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FISCAL YEAR 1973

Prepared by
Fogarty International Center

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PREFACE

This document is the fifth annual report of international activities published by the John E. Fogarty International Center for Advanced Study in the Health Sciences. It contains a comprehensive narrative review and analysis of the international activities undertaken by the National Institutes of Health in FY 1973. A companion booklet entitled "NIH International Awards for Biomedical Research and Research Training, FY 1973" lists the individual awards made under the various NIH programs.

Within this review, there are discussed in some detail the many international activities of the National Institutes of Health and their contribution toward broadening the knowledge base of the biomedical sciences dedicated to the improved health of American citizens as well as those of other nations. A significant part of the NIH international activities, including the participation of distinguished foreign scientists in the Scholars-in-Residence Program and Fogarty International Center conferences and symposia as well as bilateral cooperation, was undertaken under the auspices of the Fogarty International Center. Other activities providing for international biomedical cooperation have been conducted under the administrative purview of several Institutes and Divisions of the NIH. These organizations have contributed to the substantive content of this report with descriptive analyses of their activities, thereby providing a guide to the various types of NIH international programs.

One important aspect of international cooperation which is very difficult to quantify and which has not been included in this document is the informal cooperation and sharing of information between professional colleagues in the United States and overseas. This cooperation, of course, is as valuable to the fulfillment of the NIH mission as those other, more formal international cooperative activities described herein.

This document was prepared by the International Cooperation and Geographic Studies Branch, Fogarty International Center, Dr. Joseph R. Quinn, Chief. This branch is responsible for the overall coordination within the Fogarty International Center of activities involving other governments.

Milo D. Leavitt, Jr., M.D.
Director
Fogarty International Center

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ANNUAL REPORT OF INTERNATIONAL ACTIVITIES

It has been the policy of the National Institutes of Health for many years to stimulate and support international biomedical research. Since the end of World War II, in particular, the NIH also has sought to extend international biomedical cooperation recognizing, of course, that the exchange of data among scientists of many nations is fundamental to scientific progress. Thus, substantial research grant awards have contributed to the development of productive working relationships between the NIH and foreign laboratories. Other support of various kinds also has been instrumental in bringing foreign scientific competence to American science. Ultimately, these efforts seek to broaden the knowledge base of the biomedical sciences devoted to improved health for citizens of the United States and those of other nations.

In pursuit of these research objectives the NIH during Fiscal Year 1973 undertook numerous international activities. Included among them, in addition to the continuation of ongoing grant and training awards, were the attendance by NIH scientists at many international biomedical conferences, sponsoring international symposia and seminars on various scientific and associated biomedical problems, reception at the NIH of distinguished foreign biomedical scientists and publication of several books and papers advancing NIH research programs. The Fogarty International Center, as the point of coordination for the international activities of the NIH, initiated or was involved in a substantial part of the international cooperation in the biomedical sciences delineated in this report.

I.

THE FOGARTY INTERNATIONAL CENTER - CONCEPT AND PROGRAMS

In a speech before the Third National Conference on World Health in September 1963, Representative John E. Fogarty introduced the concept of a center which would represent "...the visible and tangible embodiment of the nation's devotion to the use of science for peaceful purposes and the good of mankind." He envisaged a study center which would "...encompass conference facilities, laboratory and study space, and the living quarters to permit the assembly for discussion, study and research of the outstanding health scientists of the world." Representative Fogarty died on January 10, 1967, before the realization of this concept. After his death, however, then Congressman Melvin Laird proposed the establishment of such a center as a living memorial to Mr. Fogarty. The Congress and the President approved this proposal and on July 1, 1968, the John E. Fogarty Center for Advanced Study in the Health Sciences became a reality.

The close of FY 1973 records the completion of the fifth year of operations for the Fogarty International Center. During the course of these years several programs have emerged as the principal activities of the Center and from which the Center has derived much of its character in attempting to fulfill the concepts of Representative Fogarty and the Honorable Melvin Laird.

Generally, the Center's programs were designed to promote advanced study in the biomedical and related sciences and to develop practical methods to utilize the knowledge thus gained to improve the health and well being of our contemporary society. The Center's programs encourage interaction, study, cooperation and collaboration within the international biomedical community and provide opportunities for study and discussion of significant research, public health, medical and biomedically related social and economic issues.

Specifically, the projects, which constitute the general programs delineated above and which have developed within the Center over the past five years, constitute a substantial spectrum of research and administrative support activities. One such program involves studies on preventive medicine which ultimately seeks to investigate fifteen areas of preventive medicine including diseases of fetal development; trauma; emergencies and emergency care; communicable diseases; gastropathy; and endocrine and metabolic diseases. Another highly relevant and successful project involves the compilation and analyses of biomedicine and health care in a number of selected countries with special emphasis upon the Soviet Union and the People's Republic of China. Several studies covering various aspects of biomedicine and health care in the Soviet Union and China have been published during the past five years and several others are planned or in progress.

Still another imaginative project undertaken by the Center is the Scholars-in-Residence program whereby distinguished scholars undertake a period of residence at the Center to engage in research, individual study and group interaction designed to produce original contributions toward advancing biomedical knowledge and to facilitate the exchange of ideas among biomedical scholars. Another project of considerable current and potential significance is that of bilateral cooperation in biomedical research with nineteen foreign countries in which the Center serves as the point of coordination in the effort for the U.S. Government. This cooperation is governed in most instances by agreements between the U.S. and other governments but sometimes through more informal bilateral arrangements. Thus far, this cooperation has yielded knowledge of foreign biomedical research and health care as well as direct contributions by foreign scientists to the advancement of American biomedical knowledge.

In addition to these programs and projects briefly described above, the Center has engaged in several administrative programs productive for the advancement of biomedical and related scientific knowledge

in the United States. Included among these programs are:

1. the Special Foreign Currency Program (PL-480) which enables the NIH to support biomedical research in "excess currency" countries abroad;
2. the International Visitors Center which serves as a focal point for the reception of foreign scientists;
3. the International Postdoctoral Fellowship Program which has provided numerous opportunities for highly qualified foreign biomedical scientists to engage in advanced research in leading research institutions in the United States; and
4. the International Education Program under which arrangements are made in the United States for biomedical training for foreign nationals receiving WHO and UN fellowships in the health sciences.

Finally, during the past five years, the Center has provided a general coordinating function for all NIH international activities including reviewing of foreign grants and contracts, publishing of biomedical data from scientific observers abroad and disseminating information to the NIH obtained from participants in international scientific conferences and symposia.

In summary, then, the Fogarty International Center for Advanced Study in the Health Sciences is attempting:

1. to promote advanced study in the health sciences through various mechanisms including holding conferences and seminars; support of scholars in residence on the NIH campus; publications; and bilateral and multilateral cooperation;
2. to identify the legal, ethical, social and economic problems that may arise from continuing biomedical research and to advance our understanding and insight into these problems; and
3. to stimulate research concepts in specific fields through interaction among the international and domestic biomedical research community.

There follows a description, in some detail, of the previously referenced FIC program and project operations during FY 1973 through which the Fogarty International Center staff sought to fulfill the several objectives set forth above.

A. THE CONFERENCE AND SEMINAR PROGRAM

The Conference and Seminar Program of the Fogarty International Center is a unique program within the Federal Government which came into being as one of the first activities of the Fogarty Center. It is designed to advance the biomedical and related health sciences through international collaboration and communication by convening conferences and workshops which bring together international experts in various aspects of health care and biomedical research for discussion, study, and research.

Through its conference program, the Fogarty International Center organizes and sponsors working conferences on current and future directions in medical, biological, behavioral and social sciences, in particular on subjects that are interdisciplinary, of international importance and of broad interest to the biomedical community. The Fogarty International Center receives extensive cooperation from academic institutions, international health organizations, and the institutes of the National Institutes of Health in identifying appropriate topics and organizing its Conference and Seminar Program.

The subjects which are currently being studied under the auspices of the Conference and Seminar Program include:

1. Health Problems of Developing Countries
2. Medical Education and Medical Care
3. Social Aspects of Advances in Biomedicine
4. Preventive Aspects of Human Health Problems
5. Environmental Health
6. Advanced Topics in Biomedical Research

The meetings sponsored by the Conference Program vary in size and formality, from workshops of half a dozen people to large symposia of 100 or more persons. Most of these meetings are held in Stone House which contains the conference facilities of the Fogarty International Center. About 70% of the results of these meetings are published, either as a conference report or as the full conference proceedings. A publication list of these reports can be obtained from the Information Officer, Fogarty International Center.

During the past year progress has been made in the review of preventive medicine practice and needs in the United States. Disease-oriented studies were designed to:

1. review the state of knowledge of the prevention and control of human diseases;
2. identify areas requiring further research including research needs for financial resources, methodology and manpower;
3. identify defects in the translation of existing knowledge to public health benefit.

Monographs in preparation encompassing the facets of the problem include the subjects of oral health, diseases of fetal development and the neonatal period, infectious diseases, diabetes and obesity. Six additional subjects will be under study during the coming year.

In an effort to coordinate divergent activities in the field of preventive medicine, the Fogarty International Center has also undertaken a cooperative program with the Association of Teachers of Preventive Medicine. This program has the following objectives:

1. To create resource material for individual departments:

To assist in administration, teaching, research and service among Departments of Preventive Medicine;

2. To define goals of Departments of Preventive Medicine: To define department mission and enhance collaborative activity among Departments of Preventive Medicine and other departments of health science schools;
3. To promote cooperative activities among Departments of Preventive Medicine: To propose national programs of joint teaching, research and service, and provide consultative services to other agencies.

Among the 12 subjects to be considered, 6 are in a definitive planning or workshop phase. It is anticipated that the series will be completed by June 1974.

To further assist in the coordination of thought within the broad area of preventive medicine, the Center has established liaison with the American College of Preventive Medicine and the Association of Schools of Public Health, and is cooperating with the Milbank Memorial Fund Commission for the Study of Higher Education for Public Health.

Conferences held during FY 1973, together with a brief synopsis of their content, were as follows:

1. Host-Environment Interactions in the Etiology of Cancer in Man-Implementation through Research, August 27 - September 2, 1972

This conference was called to examine new approaches to the epidemiological study of carcinogenesis since it is widely believed by authorities on cancer that there are environmental factors in the causation of most cancers. The conference reviewed present epidemiological knowledge concerning carcinogenesis and the role of endocrinological, nutritional, immunological, and virological factors therein. Experts on laboratory study of these questions conferred with experts on field study who deal directly with human population. By holding this meeting in Yugoslavia, it was possible to bring together scientists not only from the western world but from eastern countries as well, including the People's Republic of China, so that a beginning could be made toward gaining an international consensus on the etiology of cancer. The proceedings of this meeting were published by the International Agency for Cancer Research in May 1973.

2. International Study of Dental Manpower Systems and Oral Health Status: The Role of the Research Sociologist, October 9-14, 1972

The broad objective of this international collaborative study is to provide guidelines for the effective and efficient utilization of manpower and financial resources to meet dental health service needs. Thus, the study is designed to relate certain characteristics of dental health care delivery systems having unique manpower arrangements to selected measures of effectiveness and efficiency. Sociological survey and clinical data will be collected, and the design of the sociological

survey was the subject of the meeting. The research sociologists conferred on information to be collected, data collection procedures, and interview techniques. Epidemiologists and medical officers were also present to provide expert consultative assistance.

3. The Genetic Control of Mutation, October 16-18, 1972

This meeting was part of a series of Fogarty Center conferences devoted to problems in genetics research. Participants to this meeting examined the current status of research in the genetic control of mutation and focused attention on the most important unsolved questions and areas of controversy in this field. Topics considered included molecular systems, which enhance the fidelity of DNA synthesis, induce errors during DNA replication, and promote repair of mutational lesions. Comparisons of these systems was made among procaryote, lower eucaryote, and mammalian cells. This conference was particularly appropriate at this time since physicians are becoming increasingly aware of the considerable impact of mutation on disease prevalence in modern societies. In addition, the great number of mutagenic agents being introduced by man into the environment may make it imperative that we learn how to decrease mutation rates. Through research, the phenomena of mutational control are beginning to be explored with increasingly sophisticated genetic and biochemical probes.

Proceedings of this conference were published in May, 1973, in the journal Genetics.

4. Pharmacokinetics and Pharmacology: Problems and Perspectives, October 30 - November 1, 1972

Pharmacokinetics, which is a special area of pharmacology, deals with the time course of drug action in the body. The primary emphasis of pharmacokinetics is on determining the concentration of a drug at its site of action in the body and the time of exposure of this site to the drug. This includes the study of how the drug is taken up by the body, in which organs it is distributed, the length of time of the drug effects, and the course of degradation and elimination of the drug. Factors that will influence these concentration and time parameters include the form and route of administration, alternation of the drug in the body by degradation and interaction with other metabolites, and the physical state of the patient. Pharmacokinetics can provide a rational basis for drug administration to patients, which can lead to optimal therapeutic effects. It can be used to prescribe the most successful regimen and route of administration of drugs to patients in individual situations and to predict the effects of new, potential drugs.

The conference on pharmacokinetics dealt both with theoretical and practical aspects of the above topics and brought together experimental pharmacologists and clinical physicians. Two topics of particular interest were discussed: the application of pharmacokinetics to the practice of medicine, and the role of pharmacokinetics in the study of drug abuse. The proceedings of this meeting will be published in late 1973.

5. Symposium on Oral Sensation and Perception: Development in the Fetus and Infant, November 20-22, 1972

This symposium dealt with oral development in the fetus and infant during the time when distinctively human competencies are being achieved. Particular emphasis was placed on the development of discrimination of sensory elicitation, on the specificity and relevance of response by the infant to stimulus, and on the emergence of voluntary functions as compared with reflexive and automatic responses. Recent advances in the fields of developmental anatomy of the mouth, pharynx and brain stem and the developmental histology of their sensory receptors were also discussed. The symposium also included critical review of a movie concerning sensorimotor evaluation of the mouth and pharynx of the newborn infant. Publication of the conference proceedings will be issued at a later date.

6. International Symposium on the Control of Lice and Louse-borne Diseases, December 4-6, 1972

Louse-borne diseases, particularly typhus fever, have played an important role in human health for centuries. They continue to be an important cause of human disease, with recent outbreaks in such areas as Burundi and Ethiopia. New technological developments in diagnosis have permitted the identification of substantial infection in countries such as Mexico, Bolivia, and Tunisia. Louse-borne typhus is, in fact, endemic in substantial areas on all continents except Australia. It is thus evident that control through insecticides has not been successful, particularly in less advanced countries. Moreover, insecticide resistance is becoming increasingly apparent, and the wisdom of continued pesticide use is in question because of its contribution to environmental contamination and its toxicity to man.

At this symposium, international experts in research and control of louse-borne diseases met to reassess the problems in this area and to develop guidelines for more appropriate and workable solutions to the control of these diseases. The proceedings of the conference will be published by the Pan American Health Organization.

7. Prevention of Human Health Problems: Oral Disorders, March 5-8, 1973

This conference on control of oral health was the first of the Fogarty Center Preventive Medicine Series designed as a comprehensive review of the status of disease prevention in the United States. The status of oral health worldwide was presented in the context of prevalence and economic impact. Trends in medical care and rising cost of oral disease were discussed. Major emphasis was placed on the preventive approach to total oral health, caries and periodontal disease being principal cases in point. The development of new preventive methods was discussed at length as well as factors affecting the delivery of preventive services.

Details of the scientific content of this conference-workshop will appear in monograph form during 1974.

8. Regulation of Gene Expression in Cultured Cells, April 4-6, 1973

This meeting was concerned with regulation of the synthesis and activity of the proteins and nucleic acids which determine growth and development of animal cells. The information for production of these molecules is coded in the genes of each cell, and regulation of this information permits differentiation into specific cell types, such as liver, skin, brain, or red blood cells. In addition, loss of control of this regulation will lead to abnormal cells such as those which are malignant. Thus, study of gene regulation is essential in understanding the normal developmental biology of an animal as well as pathological processes such as cancer or the auto-immune diseases.

Two important techniques for the study of gene regulation have recently been developed, namely, somatic cell hybridization, permitting genetic analysis of the regulatory mechanism, and cell-free translation of specific messenger RNA, permitting direct study of regulation at the level of protein synthesis. An explosive yield of data can be expected and this meeting served to review current knowledge and coordinate future research in the area of regulation of growth and differentiation of animal cells. Publication of the conference proceedings is expected in the near future.

9. Prevention of Human Health Problems: Diseases of Fetal Development, April 24-25, 1973

Prevention of fetal and perinatal disease was the subject of a conference-workshop held under the aegis of the Fogarty International Center Preventive Medicine Series. The subject was introduced with data pertaining to the incidence and impact of fetal and perinatal disease. Papers dealing with embryological investigation, fetal and placental physiology, and maternal factors in fetal development were presented. Major sections were devoted to environmental factors including drugs, radiation, infection and other pollutants as well as genetic considerations in fetal deformity. Epidemiologic surveillance and improvements in obstetrical and perinatal care were emphasized. Finally, the psycho-social and legal implications of fetal abnormality were considered. It is anticipated that the formal presentation of the subject will appear in monograph form during 1974.

10. International Symposium on Metabolic Interconversions, June 5-8, 1973

International symposia on metabolic interconversions of enzymes have been sponsored by health research institutions of several countries, including Italy and Germany. This year the Fogarty International Center supported the third international symposium, which was on a subject of

considerable importance to a number of NIH Institutes in carrying out their research mission. Enzymes are large biological molecules which promote normal chemical reactions in the body, utilization of foodstuffs and catalyze other necessary functions in all organisms. As such, the study of enzymes, their mechanism of action and the results of the reaction they catalyze are of importance in biology and medicine. Practical applications of enzymology have been found in all branches of medicine both for diagnosis and for treatment of disease. Understanding of enzyme action is essential for improvement of the ability to deal with genetic disease, cancer, and a variety of major public health problems. A number of American participants from within the National Institutes of Health as well as foreign participants were invited to the meeting. The proceedings of the meeting will be published in the near future.

11. Conference on the Medical Assistant: Intermediate Levels of Health Care Personnel, June 5-7, 1973

The purpose of the conference was to provide an international forum for the exchange of information and experience in training and utilizing medical assistants with particular reference to provision of primary health care to underserved populations. Approximately half of the participants represented developing countries and the balance were from the United States.

Primary emphasis was placed upon current developments in the United States, a comparison of the U.S. experience with that elsewhere, and a consideration of those aspects of training and utilization which may improve the accessibility and quality of health care services for all underserved populations. The rapid proliferation of training programs in the U.S. has emphasized the need to examine and clarify such issues as the definition(s), training, certification and appropriate use of intermediate levels of health care personnel. The conference offered an opportunity to learn from the experience of other countries as a means for improving the design and quality of programs in this country.

A summary of the proceedings, including recommendations that might serve as a basis for future planning and policy development, will be published in the near future.

12. International Symposium on Poly ADP-Ribose, June 11-13, 1973

Poly adenosine diphosphase ribose (ADP-ribose) is a large molecule occurring in animal cells which was discovered in 1966. Since then, laboratories around the world have been investigating the structure metabolism and biological function of this novel molecule, but these properties have not been completely elucidated as yet. It is believed to interact with chromosomes in cell nuclei to restrict their activity

and, in the presence of diphtheria toxin, to inactivate one of the components involved in protein biosynthesis. This meeting, organized by a Fogarty Scholar-in-Residence, brought together international experts who are studying poly ADP-ribose for discussion of recent research and planning of future research strategy. The proceedings of the conference will be issued at a later date.

B. THE SCHOLARS-IN-RESIDENCE PROGRAM

A crucial program in the study center concept is the Scholars-in-Residence Program. This program has been designed to facilitate the work of individual scholars and the exchange of ideas among scholars, distinguished science leaders, science administrators and promising young scientists.

Individuals accepting an invitation to participate in the program are known as "Fogarty Scholars" during their period in residence. Invitations are limited to persons of distinction who, in the judgement of the Director of the Fogarty Center, his staff and advisors, have the educational and cultural background, plus research experience to make significant contributions to advanced study in the health sciences. Awards are made without regard to national boundaries.

Scholars and invited participants are not limited solely to study in the biomedical disciplines, but may also consider philosophical as well as social, economic or legal issues. The program enables each Scholar to participate in one or more of the following types of activity:

1. Individual study: The Scholar may make an assessment or a prospective study in a specific field. This approach can be directed toward the writing of a monograph, preparation of a book or scientific report. Though working primarily on an individual basis, the Scholar is encouraged to participate in other NIH workshops, conferences and seminars;

2. Group interaction: The Scholar might prefer to collaborate with other Scholars and invited consultants in considering a common topic for the purpose of developing recommendations or suggestions for the advancement of biomedical knowledge;

3. Research: At the invitation of an Insitute, the Scholar might choose to spend a portion of his time in the laboratory. As a Fogarty Scholar, however, he is encouraged to participate in Fogarty Center sponsored workshops, conferences and seminars when appropriate.

The first group of scholars who received and accepted invitations included:

1. Professor Uriel Z. Littauer, Weizmann Institute of Science, Israel
2. Dr. Ernest Singer, formerly with the Queensland Institute of Medical Research, Australia
3. Professor P. C. C. Garnham, University of London, England
4. Professor Torsten A. Teorell, University of Uppsala, Sweden
5. Professor John T. Edsall, Harvard University, United States

Reviews of the activities pursued by these Scholars during the course of their residence at the Fogarty International Center appeared in the "NIH Annual Report of International Activities, FY 1970".

During FY 1971, four additional Fogarty Scholars were in residence at the Fogarty International Center and included the following:

1. Professor Isaac Bereblum, Weizmann Institute of Science, Israel
2. Professor Jeffries Wyman, University of Rome, Italy
3. Professor Rollin Hotchkiss, Rockefeller University, United States
4. Professor Ruggero Ceppelini, University of Torino, Italy

Reviews of the activities pursued by these Scholars during the course of their residence at the Fogarty International Center appeared in the "NIH Annual Report of International Activities, FY 1971".

During FY 1972, the following five additional Scholars joined the program:

1. Professor Ragnar A. Granit, Karolinska Institute, Sweden
2. Professor Frank J. Fenner, John Curtin School of Medical Research, Australia
3. Professor Manabu Sasa, University of Tokyo, Japan
4. Professor Osamu Hayaishi, Kyoto University, Japan
5. Professor Harry Harris, University of London, England

Reviews of the activities pursued by these Scholars during the course of their residence at the Center appeared in the NIH Annual Report of International Activities.

During Fiscal Year 1973, eleven new scholars joined the program and included:

1. Professor George Klein, Professor and Head of the Institute for Tumor Biology, Karolinska Institute Medical School, Stockholm, spent three months as a Scholar-in-Residence. Professor Klein is a distinguished scientist who has made outstanding contributions in the cancer field. As a Fogarty Scholar, he presented a number of lectures and initiated and participated in seminars at the NIH in addition to engaging in limited collaborative research with his scientific colleagues in the Cancer Institute. Professor Klein plans to resume his activities as a Fogarty Scholar during the summer of 1974.

2. Professor Lars Ernster, Chairman of the Department of Biochemistry, University of Stockholm, is a recognized authority and leader in the field of biological oxidation and phosphorylation. During his three and one half month period in residence, he related closely to a number of NIH scientists, presented several lectures and participated in several seminars. Professor Ernster will return during the late spring of 1974 to continue his activities as a Fogarty Scholar-in-Residence.

3. Professor Ronald V. Christie, Former Dean and Professor, Faculty of Medicine, McGill University, Montreal, Canada, joined the program in September 1972 and remained as a Fogarty Scholar-in-Residence through May 1973. During his tenure as a Fogarty Scholar, Dr. Christie devoted the major portion of his time to writing a document on medical curricula involving a number of countries throughout the world. In addition to this writing, he was an active participant in workshops and seminars covering the broad field of medical education and was in continuous contact with the senior staff of the Bureau of Health Manpower Education.

4. Sir Sidney Sunderland, Professor of Experimental Neurology and former Dean, Faculty of Medicine, University of Melbourne, Australia, joined the program in September 1972. Sir Sidney devoted a major portion of his time to writing in the field of experimental neurology and developed a number of manuscripts and other documents for publication. With Dr. Christie, he participated in a number of conferences in the field of medical education, presented some seminars and visited academic institutions where he presented several lectures. He remained as a Scholar through May 1973.

5. Professor William A. Rushton, a neurophysiologist at Trinity College, Cambridge, England, is a distinguished scientist who has made outstanding contributions in the field of visual physiology. Professor Rushton joined the Scholars Program in September 1972 and remained through May 1973. He devoted the major portion of his time to writing and lecturing. He related rather closely to scientific colleagues in the National Institute of Neurological Diseases and Stroke where he participated in several seminars. Professor Rushton, while a Scholar, also submitted manuscripts which were published in various scientific journals.

6. Dr. Cecil J. Watson, Regent's Professor of Medicine Emeritus and Senior Consultant to the University of Minnesota Unit for Teaching and Research in Internal Medicine, Northwestern Hospital, Minneapolis, Minnesota, was a Fogarty Scholar from September through December 1972. As a Fogarty Scholar, Dr. Watson prepared several manuscripts and an extensive monograph in the field of porphyrin metabolism. He devoted a significant portion of his time in the Clinical Center to studies involving patients; he also participated in a number of seminars with his biomedical colleagues at the NIH.

7. Dr. Charles S. Davidson, Professor of Medicine, Harvard Medical School, and Director of Clinical Service (Harvard), Boston City Hospital, joined the program in December 1972 and remained through June 1973. While a Fogarty Scholar, he worked very closely with senior staff in the Clinical Center and engaged in a study of medical research and education planning for young medical scientists coming to the Clinical Center. In addition, he actively pursued his interest in liver diseases and in this capacity related very closely to patient studies at the Clinical Center. Dr. Davidson, while a Scholar, developed a comprehensive document for the Director, NIH, concerned with the training of young clinical scientists who come to the NIH.

8. Dr. Albert B. Sabin, Distinguished Service Professor Emeritus, University of Cincinnati and Professor Emeritus, Weizmann Institute of Science, joined the Scholars Program in January 1973 for a twelve-month period. In addition to lecturing, presenting seminars and relating to scientific colleagues within the NIH, Dr. Sabin devoted a major portion of his time to virology as it relates to cancer. In this capacity he worked very closely with the viral oncology group within the National Cancer Institute. Dr. Sabin is a distinguished expert in the field of virology and during the past few years has concentrated his efforts in the cancer field.

9. Professor Henryk Eisenberg, Chairman of the Department of Polymer Chemistry, Weizmann Institute of Science, Rehovot, Israel, joined the program in March 1973 and remained through September. A physical chemist of high repute, Professor Eisenberg has concentrated a great deal of his effort on biological systems. As a Fogarty Scholar, he is spending a major portion of his time writing a book entitled Thermodynamics of Solutions of Biological Macromolecules. In addition, he has consulted with his scientific colleagues within the NIH and has presented several lectures and participated in a number of conferences.

10. Dr. George B. Darling, Professor of Human Ecology, Yale University and former Director, Atomic Bomb Casualty Commission, Hiroshima, Japan, initiated his Fogarty Scholarship in April 1973. As a Fogarty Scholar, he devoted most of his time to writing and lecturing. He consulted with colleagues within the National Cancer Institute as well as government agencies in the Washington area. Dr. Darling interrupted his period of residence during July and August and return to the program in September 1973.

11. Professor Junnosuke Nakai, Professor of Anatomy, Faculty of Medicine, University of Tokyo, joined the program in late May and continued as a Fogarty Scholar through October 1973. Professor Nakai devoted a major portion of his time to laboratory collaboration in the field of neurobiology. He has a number of scientific colleagues with whom he consulted while a Fogarty Scholar. He has presented a number of lectures and participated in a number of seminars at the NIH.

The concept of convening Scholars at the NIH envisions a group of experts from various parts of the world who are willing to spend time in residence to engage in discussions among themselves and with NIH scientific staff with the ultimate objective of providing insight and intellectual stimulation which will expedite the solution of disease problems.

During FY 1973, the Scholars-in-Residence Program functioned at maximum capacity and its beneficial effect on the scientific community was readily felt. There was a continuing interchange of information and ideas between Scholars and staff. Further expansion of this program is not now visualized but it would appear that continuing it at its present level is most beneficial in terms of achieving a cohesive intellectual stimulation within the NIH environment.

C. INTERNATIONAL VISITORS CENTER

Another significant program service of the Fogarty International Center is its International Visitors Center, which serves as a focal point for the reception of scientists from abroad. The Visitors Center is responsible for developing schedules for foreign scientists and dignitaries at NIH and coordinating them with their visits to other research centers.

During FY 1973, more than 350 visitors were received by the Visitors Center, of whom 314 were from 48 foreign countries representing every continent. Japan led the list with 65 visitors, followed by the U.S.S.R. with 39, the Netherlands with 26, and the People's Republic of China with 21. Among the distinguished visitors to NIH were Dr. Halfdan Mahler, Director General Designate, WHO, Geneva; Dr. Marian Sliwinski, Minister for Health and Social Welfare, People's Republic of Poland; Sir George Godber, Chief Medical Officer, United Kingdom; Dr. Pall Sigurdsson, Secretary General, Ministry of Health and Social Security, Iceland; Dr. Abdel W. El Borolossy, Minister of Scientific Education, Arab Republic of Egypt; and Dr. Aleksandr V. Pavlov, Deputy Minister of Health in charge of Environmental Health and Sanitation, Moscow. Principal areas of inerest to the visitors were: medical science, 85 visitors; science administration, 53; laboratory science, 52; and science press, 44.

Notable among the latter category were a group of 21 journalists from the People's Republic of China whose visit on May 30, 1973, was sponsored by the American Society of Newspaper Editors, assisted by the National Committee on United States-China Relations, Inc. Their interests focused on the new cancer research program.

On June 1, 1973, six Soviet science writers visited NIH, whose tour was sponsored by the Council for the Advancement of Science Writing. These journalists, representing the leading news sources in the U.S.S.R. such

as Isvestia and Tass News Agency, probed the US-Soviet exchange programs to learn about progress in the initial year of operation. Other interests were the new U.S. cancer initiatives; and relationships between NIH, universities, and other institutions in the private health sector.

The International Visitors Center arranged 313 appointments with NIH staff, distributed 1300 publications, and filled 29 requests for local housing. In addition, the IVC provided arrangements for 17 meetings with 222 people in attendance in the International Room.

Another responsibility of the IVC is administrative management of the NIH Visiting Program, in which 353 participating scientists were brought to NIH during FY 1973. Services included assistance with housing and other living arrangements in the area, health insurance, income taxes, visas, local educational facilities, as well as preparation of appointment papers. Analysis of the program follows under a separate heading.

D. THE INTERNATIONAL POSTDOCTORAL FELLOWSHIP PROGRAM

The oldest program administered by the Fogarty International Center is the International Postdoctoral Fellowship Program which was launched by NIH several years prior to the establishment of the Fogarty Center. Its purpose is to provide opportunities for a group of carefully selected and highly qualified foreign biomedical scientists to obtain advanced research training and to participate in research under the tutelage of leading American scientists at many of the major educational and research institutions in the United States. The participants in this program, who come from various parts of the world, have made significant contributions to the research programs of their preceptors and their host laboratories. The fellows bring different points of view to research problems and sometimes introduce new and innovative methodology developed abroad; and they, typically, have a high capacity for hard work and diligent devotion to research which is reflected in their active participation in seminars and discussions and through their publications in the scientific literatures. The International Postdoctoral Fellowship Program thus advances the biomedical sciences in the United States and helps to disseminate research results and research techniques throughout the world. In FY 1973, 37 new fellowships and 49 second year fellowships were awarded. The total cost for this program was $778,000. The budget reduction from FY 1972 was due to departmental policy for the phase-out of the International Postdoctoral Fellowship Program during FY 1973 and FY 1974.

E. THE VISITING PROGRAM

The Visiting Program undertakes to obtain the participation and assistance of outstanding young scientists for specialized research as Visiting Fellows, and for singular contributions to the progress of the NIH as Visiting Associates and Visiting Scientists. Upon

returning to their respective research centers, these promising scientists will contribute materially to their excellence and productive capacities.

Under this program, NIH Institutes and Divisions invite scientists of their choice to participate in one of the three program categories; unsolicited applications are not accepted. In contrast to Visiting Associates and Scientists, the Visiting Fellow is appointed for the purpose of receiving training and it is the responsibility of the sponsor to provide educational practices commensurate with the responsibility usually assumed by university faculty members for their postdoctoral fellows. One to three years of appropriate postdoctorate education is a prerequisite for appointment as Visiting Fellow.

There were 192 Visiting Fellows, 94 Visiting Associates, and 67 Visiting Scientists from 44 countries who received NIH awards in FY 1973 under the Visiting Program.

F. THE SPECIAL FOREIGN CURRENCY PROGRAM

The NIH Special Foreign Currency (PL 480) Program is designed to extend NIH activities into the international biomedical community for the purpose of utilizing resources indigenous to "excess currency" countries. Such activities contribute to programs for the attainment of domestic goals of the Institutes and Bureaus of NIH. The program affords an opportunity for international scientific collaboration by which the talents and efforts of scientists in the U.S. and abroad are brought to bear upon biomedical science and information exchange problems of mutual importance to the respective countries. The program utilizes currencies, acquired primarily from sale of agricultural products under Public Law 480, which are excess to the immediate needs of the U.S., and thus neither contributes to the flow of dollars nor makes demands upon annual tax revenues. It is comprised of research projects selected by the individual Institutes on the basis of technical merit and the contribution which they will make to Institute research programs. All projects must represent collaborative efforts. Each must have the commitment of an intramural (NIH) or extramural (U.S. academic institution) scientist to serve as collaborator.

A number of significant developments initiated by the State Department and the DHEW occurred in FY 1973 which will alter the current nature and shape the future of this NIH program. The reduction of balances of U.S. owned currencies to the point where, in Israel in FY 1968 and in Yugoslavia in FY 1972, it became apparent that funds would no longer be available, had a severe impact upon this program and the collaboration with the biomedical science community in these countries. The full impact of the depleted funds was realized in FY 1973 when the first projects reached the end of their previously committed period of support and could not be continued because funds were exhausted.

In anticipation of this, the U.S.-Israel Binational Science Foundation was established on September 27, 1973 with each country contributing equal amounts of Israeli pounds in a total equivalent to $60 million. The income from the investment of these funds will provide for the continuation of projects and collaborations previously established under the Special Foreign Currency Program as well as some new activities.

In a somewhat parallel action the U.S.-Yugoslavia Joint Fund was established on May 18, 1973 with a total equivalent to $14.4 million from equal dinar contributions by each country. These funds, in their entirety, will be disbursed to provide continued limited support of selected projects during a phaseout period ending in FY 1976. The funds from both these sources are intended to support scientific and technology collaborations with all U.S. Government agencies.

In another major development, priority areas of mutual interest were agreed upon with Poland for future guidance in the development of collaboration under this program. The original Memorandum of Understanding between the DHEW and the Ministry of Health and Social Welfare of Poland, which established this collaborative NIH program, became effective on March 14, 1962. A revision was signed by the Secretary of DHEW and the Minister of Health and Social Welfare of Poland on March 15, 1973 during the latter's visit to the U.S. in which the following research priorities were established:

1. cancer
2. cardiovascular diseases
3. occupational health
4. maternal and child health
5. rehabilitation
6. neurologic disease
7. metabolic and endocrine disturbances
8. transplantology and nephrology
9. models of health protection organizations

The following examples of representative projects will provide an insight into productivity of the program and some of the unusual opportunities it affords.

Archeological sites available in Egypt have provided Dr. J.E. Harris of the School of Dentistry, University of Michigan, with the basis for an investigation of the rate of differential craniofacial growth and dental development of a Nubian population along the Nile over a span of 2000 years. The finding that jaws of the modern Nubian have undergone a relatively greater reduction in size than have the teeth, resulting in severe dental crowding, has established the genetic independence of tooth size and jaw size. The resource and the study are important elements of the NIDR developmental biology and oralfacial anomaly program.

A fundamental investigation of the neurophysiological processes of feeding behavior, conducted by Dr. V. N. Sharma in India, has shown that

oral, gastric and chemoreceptors have features related to sensory and metabolic signals which are distinguishable and can modulate activities of the central nervous system structures implicated in feeding. Incidental to investigations which have elucidated the neural control of receptor systems, it has been found that electrical characteristics of nerve pulses resulting from stimulating an experimental animal by perfusion with nutrient substance and distention of the stomach differ both qualitatively and quantitatively depending upon whether the animal is well fed and in good nutritional state or whether it is subject to chronic hunger and malnutrition. Such studies contribute directly to the NINDS program concerned with investigating processes of neural control which must be understood to develop therapy for diseases caused by disturbances in the central nervous system.

In Israel Dr. Shapiro at the Weizmann Institute has synthesized complex lipids labeled with radiocarbon 14C for metabolic studies of hereditary lipid storage diseases conducted by Dr. R. O. Brady of NIAMDD. With these labeled substrates the specific enzymatic defects in Gaucher's disease and Niemann-Pick disease were identified. These discoveries established the nature of the underlying metabolic disturbances in all of the ten now known lipid storage diseases from any part of the world. These procedures have been refined so that unaffected carriers of these disorders can be identified. Most significant is the fact that pregnancies can now be monitored at risk for these diseases.

Dr. W. Drabikowski's studies in Poland of the interaction of proteins of muscle filaments, composition and properties of the regulatory protein complex and the binding of calcium and other bivalent ions are contributing knowledge about the mechanisms of muscle contraction. This knowledge is essential to an understanding of the pathological states of cardiovascular disorders, of primary importance to NHLI, which supports this project. In addition, knowledge is gained of muscular activity, all concerned with programs important to other Institutes.

In Yugoslavia Dr. V. Kovacev in collaboration with Dr. S. Chernick of NIH has validated a technique for using parametrial and epididymal rat fat pads for perfusing adipose tissue in vivo. The parallel in vitro and in vivo studies which this technique has facilitated have contributed to an understanding of the roles of hormones and their interactions in fat metabolism and diabetes, which are primary responsibilities of NIAMDD.

The National Library of Medicine's collaborative critical review program, which sponsors the preparation and publication of scholarly creative analyses of research or practices in areas of current interest in the health services, is a prominent element of the NIH Special Foreign Currency Program. Among the recent publications of this program are those entitled: Surgical Lung Diseases in Childhood, Purulent and Fibrous Mediastinitis Radiological Diagnosis, Control System Diagrams in Physiology, Biology and Medicine, Modern Concepts in Hematology, The Chemical Synthesis and the Biochemical Properties of Peptidyl tRNA, and Impact of Insulin on Metabolic Pathways.

The program is further characterized in the accompanying tables, which summarize distribution by NIH organizational unit, country and subject:

Table 1

Distribution of NIH SFCP projects by Bureau, Institute and country

	Egypt	India	Israel	Pakistan	Poland	Tunisia	Yugoslavia	Total
NIAID	4	10	3	2	2	-	-	21
NIAMDD	-	8	7	-	1	-	6	22
NCI	-	7	2	-	1	-	1	11
NICHD	2	3	-	2	2	1	5	15
NIDR	1	1	3	-	-	-	1	6
NEI	1	1	-	-	-	-	-	2
NIGMS	-	5	1	1	-	-	1	8
NHLI	-	2	2	-	2	-	3	9
NINDS	1	9	3	-	6	-	11	30
NLM	3	1	3	1	6	1	5	20
BHME	-	1	3	-	-	-	-	4
TOTAL	12	48	27	6	20	2	33	148

Table 2

Distribution of NIH SFCP projects by subject area and country

	Egypt	India	Israel	Pakistan	Poland	Tunisia	Yugoslavia	Total
Infectious Diseases	5	7	-	2	1	-	-	15
Immunology, Allergy, and Arthritis	-	1	3	-	1	-	1	6
Cardiovascular, Renal and Pulmonary Diseases	-	2	1	-	2	-	2	8
Cancer	-	7	1	-	2	-	1	11
Metabolism	-	2	3	-	-	-	4	9
Nutrition	-	9	-	-	-	1	2	12
Growth and Development	2	1	1	-	-	-	1	5
Population	-	2	-	2	2	-	3	9
Dental Studies	-	1	1	-	-	-	1	3
Neurophysiological Sciences	1	7*	3	-	7**	-	10	28
Biomedical Sciences Noncategorical	1	8	8	1	1	-	2	21
Social and Behavorial Studies	-	-	1	-	1	-	5	5(NIHM)
Health Manpower Studies (BHME)	-	1	3	-	-	-	-	4
Translation and Information Dissemination (NLM)	3	1	3	1	6	1	5	20
TOTAL	12	49	28	6	23	2	37	156

*Includes 1 NIMH

**Includes 2 NIMH

G. INTERNATIONAL EDUCATION PROGRAM

The International Education Branch arranges, supervises, and evaluates the training experiences provided international health professionals in the United States studying in the health and medical sciences. The majority of those international health professionals provided this service are sponsored by the World Health Organization and other United Nations affiliated agencies or the Department of State Cultural Exchange program. Assistance is also extended to those who are self-financed or sponsored by private foundations, voluntary agencies, or foreign governments. The Branch was transferred to the Fogarty International Center from the Bureau of Health Manpower Education during Fiscal Year 1972, and FY 1973 is its first full reporting period under the Fogarty Center.

During FY 1973 the Branch processed a total of 525 requests to arrange programs. Of these, 396, or 76%, were from the World Health Organization and other United Nations affiliated agencies, 39, or 7%, were from the Department of State, and 90, or 17%, were under various other sponsorships. The table below indicates the total number of applications handled during the year, as well as the number of international health professionals who arrived in the United States for training and the number of those whose programs were carried over from the previous fiscal year.

Table 3

Applications Processed and Programs Active during Fiscal Year 1973
By Sponsors

	Sponsors			
	WHO-UN	State	Other	Total
Applications for processing carried over from Fiscal Year 1972	92	-	5	97
Applications for processing received during Fiscal Year 1973	304	39	85	428
Total applications handled	396	39	90	525
Number of international health professionals whose programs were carried over from Fiscal Year 1972	70	-	3	73
Number of international health professionals whose programs were initiated during Fiscal Year 1973	260	31	79	370
Total programs handled	330	31	82	443

Tables 4 through 6 show the academic degree levels, fields of training, and countries of origin of international health professionals whose applications were processed in Fiscal Year 1973. In Table 7 the types of institutions utilized in placing the international health professionals are indicated. In this case, however, the figures used are based on the 443 professionals who arrived in the United States to undertake their programs in Fiscal Year 1973 or whose programs were continued from Fiscal Year 1972.

Table 4

Degree Levels of International Health Professionals
Applications Processed during Fiscal Year 1973

Degree Level	Sponsors			
	WHO-UN	State	Other	Total
Doctorate (M.D., D.D.S., D.V.M., Ph.D.)	169	17	27	213
Masters	49	-	7	56
Bachelors	86	5	8	99
No degree	70	1	1	72
Unknown	22	16	47	85
Total	396	39	90	525

Table 5

Field of Training of International Health Professionals
Applications Processed during Fiscal Year 1973

Field of Training	Sponsors			
	WHO-UN	State	Other	Total
Basic Medical Sciences	25	-	6	31
Behavorial Sciences - Total	24	6	15	45
Health Education	24	6	15	45
Sociology	-	-	-	-
Clinical Medical Sciences	20	4	3	27
Dentistry	13	-	1	14
Environmental Health and Ecology	88	-	12	100
Nursing	15	1	1	17
Other Biosciences	6	-	-	6
Other Health Related Professional Fields - Total	114	22	49	185
Drug Abuse	30	1	1	32
Epidemiology	23	-	1	24
Family Planning	21	-	9	30
Health Administration	16	14	37	67
Hospital Administration	10	6	-	16
Pharmacy	-	-	-	-
Veterinary Medicine	11	1	1	13
Mental Health	3	-	-	3
Paramedical Technologies - Total	44	5	2	51
Clinical	21	5	2	28
Environmental	6	-	-	6
Public Health	17	-	-	17
Physical Sciences	1	-	-	1
Sanitary Engineering	32	1	1	33
Statistics	14	-	1	15
Total	396	39	90	525

Table 6

Countries Represented by International Health Professionals Applications Processed during Fiscal Year 1973

Country by WHO Region	Sponsors			
	WHO-UN	State	Other	Total
Region 1 - Americas				
Antigua	1	-	-	1
Argentina	8	1	-	9
Barbados	9	-	-	9
Brazil	18	6	2	26
British Honduras	1	-	-	1
Canada	2	-	-	2
Chile	11	-	-	11
Colombia	12	1	9	22
Costa Rica	-	3	-	3
Cuba	2	-	-	2
Dominica	1	-	-	1
Dominican Republic	1	1	1	3
Ecuador	2	-	-	2
El Salvador	1	-	-	1
French Guiana	1	-	-	1
Grenada	4	-	-	4
Guatemala	7	-	-	7
Guyana	8	-	-	8
Jamaica	4	-	1	5
Mexico	7	-	1	8
Nicaragua	1	-	-	1
Peru	2	1	-	3
St. Lucia, B.W.I.	2	-	-	2
St. Vincent, B.W.I.	2	-	-	2
Surinam	2	-	-	2
Trinidad and Tobago	14	-	-	14
U.S.A.	3	-	-	3
Venezuela	21	4	-	25
Total - Region 1	147	17	14	178
Region 2 - Europe				
Belgium	3	-	-	3
Bulgaria	3	-	-	3
Czech	3	-	-	3
Denmark	5	-	-	5
Finland	-	6	-	6
France	1	11	-	12
Hungary	8	-	-	8
Iceland	1	-	1	2
Netherlands	6	-	-	6
Poland	8	-	8	16

Country by WHO Region	Sponsors			
	WHO-UN	State	Other	Total
Region 2 - Europe (Continued)				
Romania	-	-	1	1
Spain	1	1	1	3
Sweden	3	-	-	3
Switzerland	1	-	-	1
U.S.S.R.	1	-	6	7
United Kingdom	3	-	1	4
Yugoslavia	1	-	3	4
Total - Region 2	48	18	21	87
Region 3 - Africa				
Cameroon	-	-	1	1
Ghana	1	-	-	1
Ivory Coast	1	-	-	1
Kenya	2	-	1	3
Niger	-	-	1	1
Nigeria	1	-	-	1
Senegal	-	-	1	1
Seychelles	1	-	-	1
Sierra Leone	1	-	-	1
South Africa	-	1	-	1
Sudan	5	-	1	6
Togo	1	-	-	1
Uganda	2	-	-	2
Zambia	-	-	1	1
Total - Region 3	15	1	6	22
Region 4 - Eastern Mediterranean				
Bangladesh	2	-	-	2
Cyprus	-	1	-	1
Ethiopia	2	-	2	4
Hashemite Kingdom of Jordan	4	-	-	4
Iran	9	-	1	10
Israel	8	-	1	9
Kuwait	-	-	1	1
Pakistan	3	1	1	5
Tunisia	-	-	1	1
United Arab Republic	6	-	-	6
Yemen	2	-	-	2
Total - Region 3	36	2	7	45

Country by WHO Region	Sponsors			
	WHO-UN	State	Other	Total
Region 5 - Southeast Asia				
Afghanistan	2	-	2	4
Burma	2	-	-	2
Ceylon	4	-	-	4
India	62	1	-	63
Indonesia	12	-	-	12
Nepal	5	-	2	7
Thailand	9	-	4	13
Total - Region 5	96	1	8	105
Region 6 - Western Pacific				
American Samoa	3	-	-	3
Australia	4	-	8	12
Japan	2	-	16	18
Malaysia	8	-	1	9
Marianas	2	-	-	2
New Zealand	5	-	-	5
Philippines	21	-	4	25
Singapore	6	-	-	6
Taiwan	-	-	5	5
Western Samoa	3	-	-	3
Total - Region 6	54	-	34	88
TOTAL - All Regions	396	39	90	525

Table 7

Institutions Utilized by International Health Professionals
Active Programs in Fiscal Year 1973*

Institutions	Sponsors			
	WHO-UN	State	Other	Total
Academic - Total	45	-	9	54
Schools of Dentistry	7	-	1	8
Schools of Engineering	2	-	-	2
Schools of Medicine	5	-	6	11
Schools of Nursing	-	-	-	-
Schools of Public Health	1	-	2	3
Other Collegiate Placements	30	-	-	30
Governmental - Total	111	22	19	152
Federal	95	21	15	131
State	10	-	-	10
Local	6	1	4	11
Private Sector	18	-	4	22
Travel**	156	9	50	215
Total	330	31	82	443

* Foreign health professionals who either arrived in the United States during Fiscal year 1973 to undertake program or who continued program from Fiscal Year 1972.

** Travel involves multi-site visits to institutions included in a combination of the categories-academic, governmental, and private sector.

The International Education Branch also assists the World Health Organization by performing supportive and staff functions related to the selection of candidates for short-term fellowships for travel abroad. A certain number of these fellowships are awarded each year to U. S. citizens in the expectation that the experience will improve and expand health services in this country. For Fiscal Year 1973 the Branch received 554 inquiries concerning the fellowships, sent out 135 applications, received and reviewed 64 completed applications, and approved 42. Combined, the fellowships provided more than 84 months of travel in countries in all six WHO Regions. Among the proposals were included subjects such as public health control of hypertension, community and nationalized health care delivery systems, health hazards from sanitary landfills, efforts to deinstitutionalize the mentally retarded, cardiovascular fitness of elementary school boys, population control and family planning, delivery of school health care, comprehensive care for terminal illness, and immunology of malignant diseases. Table 8 shows the number of Fellows, their states of origin, field of training, duration of program, and number of visits made to each of the WHO Regions while Table 9 indicates their professions and sex.

For a number of years the International Education Branch has maintained an office in New York City. While the workload handled by that office has increased steadily, it has risen to alarming proportions during the past year. This area is the center of a great number of resources used by the Branch and is also the port-of-entry of a large portion of international visitors. The New York office has especially been helpful in cooperating with the Office of International Health, the Agency for International Development, and the Cultural Exchange Program of the Department of State in preparing programs for their many international visitors. Of special interest during the year were visits by participants in both the US-USSR Agreement for Cooperation in Health and the US-Romania Health Exchange whose programs were prepared by our New York representative for the Office of International Health. Another program was prepared for the team from the Polish Ministry of Health.

The Branch continues to be of all service possible to organizations and agencies working in the field of international health. One of its staff has been detailed to the Office of International Training of the Agency for International Development to assist in programming AID-sponsored health participants. This detail, begun in September 1972, has been extended into Fiscal Year 1974. During Fiscal Year 1973 the Branch was also able to offer assistance to such diverse organizations as the International Planned Parenthood Federation, the Australian National Health and Medical Research Council, the Foreign Students Service Council, the World Bank, the Winston Churchill Travelling Fellowship program, the Japan Productivity Center, the Eisenhower Fellowship program, and the Governmental Affairs Institute.

Table 8

World Health Organization Fellowships Awarded to United States Citizens in 1973

No. of Fellows	States of Origin (United States)	Field of Training	Duration (Months)	WHO Regions Visited*						Total Number of Visits
				1	2	3	4	5	6	
15	Calif., Ill., Ks., La., Mo., N.J., N.Y., Pa., Wisc.	Medical and Health Training	30	2	8	2	4	-	1	17
2	Ga., Ind.	Hospital Administration	3	1	2	-	-	-	-	3
16	Ariz., Calif., Hawaii, Ks., Mich., N.H., N.Y., Puerto Rico, S.C., Tenn., Va.	Public Health Administration	35	1	15	-	-	-	1	17
1	Calif.	Nursing Education	2	-	-	1	-	-	-	1
1	N.M.	Epidemiology	2	-	1	-	-	-	-	1
2	Ala., Minn.	Veterinary Medicine	4	-	1	-	1	1	-	3
1	Mass.	Environmental Health	2	-	1	-	-	-	-	1
3	Calif., Colo., Ill.	Medical Care	4	-	3	-	-	-	-	3
1	Calif.	Medical Social Work	2	-	1	-	-	-	-	1
42	24 States		84	4	32	3	5	1	2	47

*WHO Regions are as follows: 1 - Americas; 2 - Europe; 3 - Africa; 4 - Eastern Mediterranean; 5 - Southeast Asia; 6 - Western Pacific.

Table 9

Recipients of World Health Organization Fellowships in 1973
By Profession and Sex

Profession	Governmental		Teaching		Other		Total	
	Male	Female	Male	Female	Male	Female	Male	Female
Dentist	1	-	-	-	-	-	1	-
Education - Total	-	-	9	-	-	-	9	-
Health Administration	-	-	1	-	-	-	1	-
Hospital Administration	-	-	1	-	-	-	1	-
Medical	-	-	3	-	-	-	3	-
Public Health	-	-	2	-	-	-	2	-
Sociology	-	-	2	-	-	-	2	-
Engineer	-	-	1	-	-	-	1	-
Epidemiologist	-	1	-	-	-	-	-	1
Health Administrator	-	-	-	-	1	-	1	-
Health Educator	-	1	-	-	-	-	-	1
Hospital Administrator	1	-	-	-	3	-	4	-
Medical Social Worker	-	1	-	-	-	-	-	1
Nurse	-	-	-	2	-	-	-	2
Physician	10	1	4	1	2	-	16	2
Research Associate	-	-	-	-	1	-	1	-
Veterinarian	-	-	2	-	-	-	2	-
Total	12	4	16	3	7	-	35	7

H. THE GORGAS MEMORIAL INSTITUTE

The Gorgas Memorial Institute of Tropical and Preventive Medicine was founded in 1921 as a living memorial to Major General William Crawford Gorgas whose efforts in environmental sanitation led directly to this nation's successful construction of the Panama Canal and to the virtual eradication of yellow fever from the great urban centers of tropical America. The Congress of the United States charged this Institute with the broad mission of improving the health and well-being of the people of Latin America. To that end, and with the continuous direct support from the Congress, the Institute has operated the Gorgas Memorial Laboratory in Panama City, Republic of Panama.

From its inception, the laboratory has concentrated its efforts toward the investigation and control of a variety of infectious diseases of particular tropical significance. Some of the major accomplishments include demonstration of the efficacy of new antimalarial drugs, first large-scale use of residual spraying of DDT, adaptation of human malaria parasites to certain simian hosts and recognition of the prevalence and public health importance of Chagas' disease (American trypanosomiasis). Intensive study of virus diseases has elucidated the natural history of Venezuelan equine encephalomyelitis and sylvatic yellow fever. Major emphasis has been placed on the study of deranged ecology, the current example being a multifaceted investigation of health repercussions of the Bayano River impoundment.

In 1970, the Fogarty International Center assumed responsibility for the Congressional justification of Institute programs and subsequently encouraged a new interest in scientific advisory activities relating to program review and development. In 1972, the Institute acquired responsibility for the operation of the Middle America Research Unit (MARU), a field laboratory of the National Institite of Allergy and Infectious Diseases. This organization has developed especially as a virus research center and has gained international respect for its work on such diseases as hemorrhagic fever, equine encephalitis and hepatitis carried out in several countries of Latin America. Although MARU operations are presently financed by annual temporary contracts with NIH, stable financing of this component is a matter of some urgency.

Economic and social evolution have resulted in changing disease patterns which require broadening the scope of research activities in Latin America. Thus, in addition to vector-borne diseases, major emphasis should be placed on the interrelationship of environmental factors, economic development, and the major health problems of artherosclerosis, hypertension, various cancers and nutritional disorders.

I. BILATERAL AGREEMENTS FOR COOPERATION IN BIOMEDICAL RESEARCH

1. General Agreements in Science and Technology:

During FY 1969 and FY 1970, efforts were undertaken to expand biomedical

cooperation with other governments. This new effort involved programs for biomedical cooperation within existing or newly negotiated bilateral general science agreements which, while deliberately drafted to embrace a wide spectrum of scientific areas, encourages cooperating governments to share the cost of research. Expenditures in the cooperating country would be paid for by that government and those in the United States by the American Government. Over the past several years these arrangements provided additional vehicles to utilize that reservoir of scientific and technical biomedical personnel abroad who have contributed to the advancement of the world's biomedical knowledge.

These bilateral agreements for cooperation in science and technology generally developed as a result of a mutual desire to cooperate in scientific and technological research. A visit to the other country concerned by a team of specialists from several fields of science and technology usually initiated the negotiation of the agreement.

Since these arrangements are very general in nature, the Department of State usually designated one agency of the United States Government to act as "executive agency" in coordinating implementation of these accords. In one instance the Smithsonian Institution was designated and in other cases the National Science Foundation was designated "executive agency". According to implementing guidelines, if a cooperative biomedical research project is developed by a participating agency such as NIH under one of these general agreements, the project application is submitted to the United States executive agency and its foreign counterpart agency for approval.

To date, under the aegis of these agreements, a number of biomedical cooperative projects have been proposed and several exchanges have taken place between American and foreign biomedical scientists. During FY 1973, although discussions continued with a number of the countries with which the United States has bilateral agreements, cooperative activities in the biomedical and health sciences were limited to a relatively few. The countries involved in these cooperative activities were France, Germany, Israel, Italy, Japan, Poland, the U.S.S.R. and Yugoslavia. There follows brief synopses concerning biomedical cooperation between the U.S. and these countries in FY 1973.

a. France

Implementation of Franco-American biomedical cooperation continued during FY 1973 in the several areas in which progress occurred during the two previous years. Research personnel were exchanged and scientific discussions were held. These areas, which were agreed upon by senior American and French health administrators in 1970, along with the principal scientific coordinators and the visitors to the respective laboratories, are included in the table recorded immediately below.

U.S. - French Biomedical Cooperation Under
the Bilateral Agreement for Cooperation

	Project Title	U.S. Investigator	French Investigator
1)	Hormone and Cancer	Dr. Edward V. Jenson, Director, Ben May Laboratory for Cancer Research, Chicago	Prof. E. E. Baulieu Hospital de Bicêtre

a) French Scientists Visiting the U.S.:

M. A. Plas, Research Unit on Molecular Metabolism and Physiopathology of Steroids at Bicêtre visited the Ben May Laboratory for two weeks beginning February 5, 1973.

b) U.S. Scientists Visiting France:

None in FY 1973.

2)	Cellular Microirradiation, experimental ultrastructural	Dr. Wallace N. Jensen, Chairman, Dept. of Medicine, George Washington University and Dr. G. Brecher, University of California, San Francisco	Professor M. Bessis Institut de Pathologie Cellulaire, Bicêtre

a) French Scientists Visiting the U.S.:

Professor M. Bessis, Director of the Research Unit of Cellular Pathology at Bicêtre, visited several U.S. laboratories in New York, Rochester, St. Louis, San Francisco, and Washington from May 12 to May 30, 1973.

Dr. C. Feo, Research Unit of Cellular Pathology at Bicêtre, attended the symposium of the American Red Cross and visited several U.S. laboratories for conferences between May 1 and 15, 1973.

b) U.S. Scientists Visiting France:

Dr. R. I. Weed visited the Research Unit of Cellular Pathology at Bicêtre from March 25 to May 1, 1973.

Dr. James Haley, University of California, visited the Research Unit of Cellular Pathology at Bicêtre from June 24 to July 31, 1973.

Professor G. Brecher, University of California, San Francisco visited the Research Unit of Cellular Pathology at Bicêtre in September 1973.

	Project Title	U.S. Investigator	French Investigator
3)	Histocompatibility	Dr. Bernard Amos, Chief Dept. of Immunology, Dept. of Microbiology, Duke University School of Medicine, Durham, N.C.	Dr. Herve Betyel, Centre to Transfusion Sanguine

a) French Scientists Visiting the U.S.: None.

b) U.S. Scientists Visiting France:

Dr. Milo B. Alter, University of Wisconsin, Madison, Wis. visited the Research Unit of Immuno-genetics of Human Transplantation in Paris from May 1 through June 8, 1973.

4)	Antigen Systems of Leukemia and Tumors	Dr. John B. Moloney, National Cancer Institute	Prof. G. Mathé, Hospital Paul Brousse, Villejuif

a) French Scientists Visiting the U.S.:

Dr. J. C. Chuat, Laboratory of Experimental Hematology in Paris, visited the NCI in Bethesda from March 14 to March 29, 1973.

b) U.S. Scientists Visiting France:

Dr. M. Ablashi visited the International Center for Cancer Research in Lyon from April 11 to June 16, 1973.

5)	Neonatology	Dr. Norman Kretchmer Stanford University	Prof. A. Minkowski, Cochin Maternity Hospital, Paris and P. Doyer, Paris and others

a) French Scientists Visiting the U.S.:

Madame Swierczwski, Research Unit of the Neonatology Laboratory in Paris visited the School of Medicine at Stanford University, Palo Alto, between September 15 and December 15, 1972.

Professor Minkowski, Director of the Research Unit of Neonatology Biology in Paris, visited the School of Medicine, Stanford University, Palo Alto in June 1973.

Madame J. B. Roux, Research Unit of Neonatology Biology in Paris visited the School of Medicine, Stanford University, Palo Alto during April 1973.

b) U.S. Scientists Visiting France:

Professor N. Kretchmer, School of Medicine, Stanford University, Palo Alto, visited the Research Unit of Neonatology Biology in Paris from October through December 1972.

Dr. N. Hoogenraad, School of Medicine, Stanford University, Palo Alto, visited the Research Unit of Neonatology Biology in Paris from October through December 1972.

	Project Title	U.S. Investigator	French Investigator
6)	Basic Reactions of Pulmonary Tissues to Inhaled Pollutants	Dr. Douglas H. K. Lee, NIEHS	Prof. P. Sadoul, Unité de Recherches des Physiopathologie Respiratoire, Nancy

a) French Scientists Visiting the U.S.:

Dr. Q. T. Pham, Research Unit of the Laboratory of Physio-pathology of Breathing, visited the NIEHS laboratories in Bethesda for six weeks beginning on April 28, 1973.

b) U.S. Scientists Visiting France:

Dr.J.H.Knelson, NIEHS laboratories in Bethesda, visited the Research Unit of the Laboratory of Physio-Pathology of Breathing in Nancy, from February 12 to March 10, 1973.

7)	Thyroglobulin Synthesis and Thyroglobulin Structure	Drs. J. E. Rall, J. Robbins and J. Wolff, NIAMDD	Professor S. Lissitzky Faculty of Medicine, Marseilles

There was no exchange of scientists during FY 1973.

	Project Title	U.S. Investigator	French Investigator
8)	Myeloma Proteins	Dr. Henry Metzger, NIAMDD	Professor N. Seligman Hôspital Saint Louis, Paris

There was no exchange of scientists during FY 1973.

9)	Central Mechanisms	Dr. C. D. Clemente Dept. of Anatomy, University of California, Los Angeles	Prof. Michele Jouvet, Hôspital Neurologique, Lyon

There was no exchange of scientists in this project during FY 1973.

In addition to the exchange of scientists set forth above, French and American research scientists cooperated in developing several articles in the areas of histocompatibility, antigen systems of leukemia and tumors, neonatology and central mechanisms. These articles were published in European and American biomedical journals, including Transplantation, European Journal of Immunology, The Journal of Experimental Medicine, and the Journal of Biological Chemistry.

b. Germany

A group of German scientists, concerned with the development of "circulation and circulation-assist devices", visited U.S. research institutions involved in research on this subject in February 1972.

In reciprocation, a group of U.S. physician-scientists visited Germany in November 1972 for the purpose of exploring the status of research in Germany in this same field. Their two week visit included discussions with eight German research and development groups concerning background information on the requirements, type, status and composition of the German cardiovascular research programs. Among the German organizations visited were the Biotechnical Laboratory, West Berlin; AEG-Telefunken in Hamburg; the Technical University of Aachen; University of Duesseldorf; the Institute of Biomedical Techniques, University of Erlangen; and the Gesellschaft fuer Strahlen und Umweltforschung m.b.H. at Neuherberg near Munich.

The visit afforded this group of American physicians a very informative view of the German cardiovascular program, especially the work underway in circulatory assist and heart replacement research. At the conclusion of the visit it was agreed between the American scientists and their hosts that efforts would be made in the future to increase scientist-to-scientist exchange of information but without government participation.

c. Israel

On September 27, 1972, Secretary of State, Mr. William Rogers, and the Israeli Finance Minister, Mr. Pinhas Sapir, signed an agreement establishing the United States-Israeli Binational Science Foundation. The Foundation, whose base of operations will be in Israel, is to be a permanent institution to promote cooperation between the U.S. and Israel to further research in science and technology for peaceful purposes on subjects of mutual interest. It is anticipated that biomedical sciences will represent a prominent part of this bilateral cooperation.

The U.S. and Israel will each provide the equivalent of $30 million Israeli pounds for the Foundation's endowment. The U.S. contribution will consist of pre-payments by Israel of PL-480 loans which were due in the period 1988-2001. A Board of Governors consisting of ten members, five appointed by each government, will determine the areas for

cooperative research programs, and the Foundation's financial and managerial policies. The Board will normally meet once a year in Israel.

In the years prior to the signing of this agreement, U.S. cooperation with Israel in the biomedical sciences funded by the PL-480 program (See Section F, Special Foreign Currency Program) has produced significant biomedical research results such as epidemiological findings in coronary heart disease. Additional biomedical projects are anticipated under this new agreement in future years.

d. Italy

The United States-Italy Science Agreement, signed in 1967, is a general "umbrella" agreement for scientific cooperation within which specific biomedical projects have been incorporated since FY 1970.

During FY 1973, as with previous years, several on-going and new projects were recommended by the NSF to be included within the above "umbrella" agreement. The following list delineates these projects, the principal researchers and institutions and includes those projects which are now incorporated within the "umbrella" agreement and those that are pending approval either by U.S. agencies or the CNR (Conseglio Nazional delle Recherche). The projects are listed under the institute through which they derive support.

U.S. - Italy Biomedical Cooperation Under
the Bilateral Agreement for Cooperation

1) National Institute of Arthritis, Metabolism and Digestive Diseases

	Project Title	U.S. Investigator	Italian Investigator
a)	Biochemical and Genetic Studies on the structure of Histidyl tRNA Synthetase and on the Methylation of Histidine tRNA	Dr. Bruce N. Ames, University of California, Berkeley	Prof. Francesco Salvatore, University of Naples
b)	Mechanisms of Glucose Transport and the Action of Insulin	Professor Pedro Cuatrecasas, Johns Hopkins University	Dr. Gennaro Illiano University of Naples
c)	Structure and Biosynthesis of Thyroid Iodoproteins	Dr. H. Edelhoch, NIH	Prof. G. Salvatore, University of Naples

	Project Title	U.S. Investigator	Italian Investigator
d)	Mechanisms of Repression of Biosynthetic Pathways in Histidine Operon	Dr. Robert F. Goldberger, NIH	Dr. Francesco Blase, University of Naples
e)	Purification and Characterization of Human Glycosidases	Dr. Y. C. Lee, Johns Hopkins University	Dr. G. Romeo Institut International
f)	Aging of the Skin	Dr. William Montagna, Oregon Regional Private Research Center	Prof. Ferdinando Serri, University of Pavia
g)	Metabolic Effects of Acid Base Disorders	Dr. Arnold S. Relman, University of Pennsylvania	Dr. Alberto Tizianello, University of Genoa
2)	National Cancer Institute		
a)	Characterization of the Viral Genome Products (RNA and Proteins) Expressed by Cells Transformed by Mammalian RNA Tumor Viruses	Professor Maurice Green, St. Louis	Prof. Giancarlo Vecchio, University of Naples
b)	The Role of Cyclic Nucleotides in the Regulation of Gene Expression and Protein Synthesis in Animal Cells	Dr. Ira Pastan, NIH	Dr. Stelio Verrone, University of Naples
c)	Antigenic and Chemical Characterization of Cells Transformed by Adenoviruses	Dr. Fred Rapp, Penn. State University	Dr. Sergio Pauluzzi University of Perugia
3)	National Eye Institute		
	Interhemispheric Integration of Visual Perception and Learning	Dr. James M. Sprague, University of Pennsylvania	Prof. Giovanni Berlucchi, University of Pisa

4) National Institute of General Medical Sciences

Radiolysis of Some Biochemical Substances	Prof. George Gorin, University of Oklahoma	Prof. Marcello Quinteliani, Fotochimia Laboratories

5) National Heart and Lung Institute

a)	Development of Physio-Chemical Techniques of Biological Interest	Dr. R. L. Berger, NIH	Dr. L. Rossi Bernardi, University of Milan
b)	Cell Metabolism Susceptibility to Injury and Disease	Dr. Paul E. Carson, University of Chicago	Dr. Franco Ajmar University of Genoa
c)	Basic Mechanisms Underlying Erythropoiesis	Dr. Albert S. Gordon, New York University	Dr. Cesare Peschle, University of Naples
d)	Relationship Between the Metabolism of Triglycerides and Myocardial Function	Dr. Niels Haugaard and Dr. Marilyn Hess, University of Pennsylvania	Dr. Adalgiso Bizzi and Dr. Silvio Garattini, Istituto di Ricerche
e)	Bioengineering Analysis of Microvascular Function	Dr. Marcus Intoglietta University of California, San Diego	Dr. Rodolfo Monti, University of Naples
f)	Thermal and Potentiometric Analysis of Proteins*	Dr. Mario Marini, Northwestern University	Dr. Mario Forlane, University of Rome
g)	Hemoglobin and Myoglobin Kinetic Studies	Dr. Lawrence J. Parkhurst, University of Nebraska	Prof. Guiseppe Ceraci, CNR, Naples
h)	Chemistry, Morphology, and Biological Activity of the Pulmonary Surfactant System in the Fetus and Adult, Normal and Abnormal	Dr. Emile M. Scarpilli, Yeshiva University	Dr. Ermelando Cosmi, University of Rome

*These projects are awaiting concurrence from the CNR

	Project Title	U.S. Investigator	Italian Investigator
i)	New Modifications for Mechanical Ventricular Assistance	Dr. David B. Spinner, Johns Hopkins University	Dr. Sergio Stipa, University of Rome

6) National Institute of Mental Health

Studies in Laterality	Dr. Herman A. Wilkin, Education Testing Service	Prof. Liugi Pizzamiglio, University of Rome

7) National Institute of Neurological Diseases and Stroke

Synaptic Organization of the Retina*	Dr. Arnaldo Lasanski, NIH	Dr. Pier L. Marchiafava, CNR

e. Japan

During FY 1973 the U.S.-Japan Cooperative Science Program, established in 1960 to foster a closer collaboration between scientists of the two nations, included within its program eight biomedical research projects. These projects were supported wholly or in part by the NIH and included the following projects:

	Project Title	U.S. Investigator	Japanese Investigator

1) National Eye Institute

Mechanism of Eye Movement and Their Nervous Controls	Paul Bach-y-Rita, U. of Pacific	Fumio Ito, Aichi-Gakium U.

2) National Heart and Lung Institute

a)	Pathophysiological and Physiochemical Studies on Tetinol Binding Protein in Chronic Cadmium Poisoning	DeWitt S. Goodman, Columbia University	N. Hosoya, U. of Tokyo
b)	Respiratory Regulation of Chronically Denervated Subjects	J.W. Severinghaus, U. of California, San Francisco	Shohei Watanabe, Chiha U.

*These projects are awaiting concurrence from the CNR

	Project Title	U.S. Investigator	Japanese Investigator
c)	Magnetic, Optical and Kinetic Properties of Hemoproteins	Takashi Yonetani, U. of Penna.	Banji Higehara, Osaka U.
d)	Cardiac Prosthesis	T. Atutsu, U. of Miss.	K. Atsumi, U. of Tokyo

3) National Institute of Neurological Diseases and Stroke

Motor Control	Fred Horvath, N.Y. Med. College	K. Kubota, Kyoto U.

4) National Institute of Arthritis, Metabolic and Digestive Diseases

Thyroid Function in Molar Pregnancy	Ronald Arky, Harvard U.	Kiku Nakao, U. of Tokyo

5) National Cancer Institute

Biochemistry of Ecdysones	Walter J. Burdette U. of Texas	Tsunematsu Takemoto, Tohoku U.

f. Poland

On March 15, 1973 the Secretary of DHEW, Mr. Weinberger, and the Minister for Health and Social Welfare, Government of Poland, Dr. Marian Sliwinski, signed a memorandum of Understanding for Cooperation in the Health Sciences. This memorandum of Understanding supersedes one signed in 1962 which was limited to activities funded with U.S. owned "excess" foreign currency (see section F, Special Foreign Currency Program).

The new agreement identifies other mechanisms that are not entirely dependent on such funding. These include: joint research between collaborating laboratories and institutions; exchange of scientific and technical publications; exchange visits of scientists; organization of scientific symposia and conferences; and the exchange of materials, drugs and biologicals.

In addition, the agreement focuses future cooperative efforts on jointly determined priority areas. Nine such areas have already been identified. These include: cancer, cardiovascular diseases, occupational health, maternal and child health, rehabilitation, neurologic diseases, metabolic and endocrine disturbances, transplantation and nephrology, and models of health protection organizations.

g. U.S.S.R.

For well over a decade, beginning in 1958, the U.S. and the Soviet Union have engaged in cooperative efforts in the fields of public health and medical sciences through exchanges of biomedical personnel, scientific correspondence and joint scientific symposia. Cancer, cardiovascular diseases, rheumatic diseases, and infectious and virus diseases are those areas which have been most prominently featured in U.S.-Soviet cooperative ventures during the past several years.

In March, 1972 a new five year U.S.-U.S.S.R. Agreement on Health Cooperation was initialled and later formalized when it was signed in Moscow on May 23, 1972. This new agreement provided that prior fields of cooperation would be continued and additional specific areas concerning cardiovascular, cancer and environmental problems would be delineated for more intensive and accelerated cooperative efforts. This agreement also provided for the creation of a binational committee (Joint U.S.-Soviet Committee for Health Cooperation) to make policy, evaluate progress and maintain general supervision through regular meetings. The American committee members consisted of Dr. Roger O. Egeberg, Co-Chairman, the Director of the Office of International Health, DHEW, who served as Deputy Co-Chairman, and the Directors of the NHLI, NCI, and NIEHS. The Soviet members held corresponding positions in the Soviet Government and Ministry of Health.

The Joint Committee held its initial meeting in Moscow during the last week of March, 1972, and agreed on the following specific problems for collaborative research:

1) Cardiovascular Diseases

Problem
a) - Pathogenesis of Arteriosclerosis
b) - Ischemic Heart Disease
c) - Myocardial Metabolism
d) - Congenital Heart Disease
e) - Sudden Death
f) - Cardiovascular Surgery

2) Environmental Health

Problem
a) - Biological Effect of Inhaled Chemicals
b) - Biological Effect of Orally Introduced Chemicals
c) - Complex Biological Effects of Chemicals
d) - Scientific Basis of Biological Effects

3) Oncology

Problem a) - Chemotherapy
b) - Immunotherapy
c) - Leukemia and Tumor Viruses
d) - Genetics of Tumor Cells

At its second annual meeting held in Washington and at the NIH in Bethesda, Maryland, the conferees agreed on strengthening collaboration in the three major areas: cardiovascular diseases, environmental health and cancer. In addition to stressing the need to strengthen collaboration in the three major areas above, it was agreed that a problem be developed on the organic basis of schizophrenia and that other areas of potential collaboration be investigated. A Memorandum of Agreement setting forth in detail the above principles was signed by Drs. Egeberg and Venediktov on March 30, 1973 (see Section K for more details of the meeting, the Memorandum of Agreement and protocols and plans for an expanded cooperative program).

During the year between the two meetings of the Joint Committee, representing most of FY 1973, there was substantial collaboration between the health scientists of the two countries toward fulfilling the objectives set forth in the five year agreement of March 1972. There were over 100 U.S. and Soviet health scientists who visited and worked in each other's country, including an American team on cancer chemotherapy that visited the Soviet Union in June and July 1972 to discuss the details of clinical chemotherapy protocols and the evaluation of the hazardous effects on man of chemicals in the environment.

As a result of the visit of this cancer chemotherapy team, cancer chemotherapeutic agents, cancer viruses and viral reagents were exchanged in a cooperative effort directed toward identifying and characterizing these viruses. As a result of consultation among still other biomedical scientists, bilateral clinical and laboratory projects were also initiated in the areas of cardiovascular diseases and malignant neoplasms. Laboratory equipment and therapeutic instruments were also exchanged.

h. Yugoslavia

On May 18, 1973 representatives of the U.S. and Yugoslavia signed an agreement providing for joint financing of cooperative science and technology projects. Under this agreement both governments will undertake to encourage organizations and institutions to continue with present forms of cooperative projects and to develop new means and sources of financing.

As part of the agreement there will be established the U.S.-Yugoslavia Board on Scientific and Technological Cooperation to approve new projects, allocate funds and provide appropriate guidance to the cooperative program.

For several years prior to the signing of this agreement, the U.S. and Yugoslavia have cooperated to promote biomedical projects of mutual interest funded by the PL-480 program (see Section F, Special Foreign Currency Program). Included among these projects were studies on the

epidemiology of heart disease. It is anticipated that additional, relevant, biomedical projects will be promoted under the aegis of this new agreement.

2. Other Intergovernmental Activities

a. Sweden

Although there is no general "umbrella" agreement for scientific cooperation and technical exchange between the United States and Sweden relating to biomedical programs, there have been periodic visits and discussions between American and Swedish health scientists for many years.

During FY 1973 American and Swedish health scientists held a Continuing Workshop on Drug Metabolism, Clinical Pharmacology and Toxicology on January 19 and 20, 1973. The major purpose of the Continuing Workshop was to encourage scientists to engage in collaboration.

The objectives of the informal workshop were to provide an interchange of information including unpublished data, identification of research frontiers, planning of prospective research and implementation of personal contacts. The workshop was conceived to be a continuing relationship with meetings alternating between U.S.A. and Sweden on a two year basis probably with a rotating membership.

The first workshop meeting held on January 19-20, was undertaken through the joint sponsorship of the National Institutes of Health and the Swedish Medical Research Council. The major portion of the one and one-half day meeting was held in the John E. Fogarty International Center for Advanced Study in the Health Sciences, National Institutes of Health.

The organizers and co-chairmen of the meeting were Dr. Bo Holmstedt, Professor, Department of Toxicology, Swedish Medical Research Council, Karolinska Institute and Dr. Byron B. Clark, Director Pharmacology-Toxicology Program, National Institute of General Medical Sciences. The attendees of the meeting numbered ten participants and one observer from Sweden and nineteen participants from the U.S., as well as approximately ten observers from the NIH.

There were four major topics discussed:

1) Analytical Methodology
2) Relation to Dose and Plasma Levels of Drugs and/or Metabolites to Therapeutic or Adverse End Points
3) Perinatal Pharmacology and Toxicology
4) Toxicology

Following presentations and discussions on the above topics, there was a summary of the highlights of the meeting led by Dr. Bo. Holmstedt.

b. United Kingdom

Joint National Institutes of Health-Medical Research Council Conference: Applications of Statistics and Computing to Medicine

The purpose of this conference, held at the Ciba Foundation, London, on May 21-25, 1973, was to explore the mutual interests of the U.S. and U.K. governmental health organizations in the application of computers and statistical methods to health and medical problems, and to define possible collaborative efforts in this field. Participation was limited to approximately 25 individuals of whom eight were from the NIH.

The following is a brief review of topics discussed and those singled out for further study by collaborative teams. The following general areas were discussed:

1) Physiological and pathological signal processing

   a. Electrocardiography

2) Image processing and pattern recognition

3) Clinical decision-making

4) Medical record management

5) Mathematical and statistical problems

In addition a short session was held on nuclear medicine. Clinicians on both sides contributed to all discussions.

At the time of preparation of this report, two collaborative projects are in being or soon to be so. J. Prewitt (NIH) and D. Rutovitz (MRC) have been working together on general problems of automated image analysis. Starting in September, E. K. Harris (NIH) will be collaborating with M. J. R. Healy (MRC) on applications of time series analysis to clinical research data and to quality control in clinical laboratories. It is expected that B. Mac A. Sayers and T. Williams of the MRC will also be consulted in these projects. Another potentially useful collaborative project includes J. J. Bailey (NIH) and P. McFarlane (MRC, Glasgow) on further development of automated ECG analysis. A closer working relationship between the efforts of C. C. Spicer's group (MRC) and T. L. Lewis (NIH, C.C.) in the implementation of computer-based medical records and hospital information systems appears worthwhile to both sides and agreeable to the individuals concerned.

This conference was unquestionably successful in its basic purpose of exploring areas of common interest, discussing current progress and projects, and establishing professional ties.

J. GEOGRAPHIC HEALTH STUDIES

As suggested by the bilateral programs, the scientists and science administrators of the National Institutes of Health are actively seeking to expand their knowledge of foreign health activities and programs as another mechanism for providing new insights for the improvement of the health of the American people. The Fogarty International Center, as the focal point for the international activities of the NIH, is uniquely situated to keep abreast of the progress of foreign biomedical activities. These activities, of course, include biomedical research, medical education, health manpower and health systems.

Continuing dialogue among clinicians and scientists of many parts of the world, particularly those in the Western Hemisphere, Western Europe and Japan, in the past, has enabled a relatively easy exchange of national biomedical data. In certain areas of the world, however, several barriers such as language differences, geographic inaccessibility, and cultural variations, have inhibited more fruitful exchanges of information. In an effort to improve the existing situation, the Fogarty International Center has initiated a series of studies concerning the several aspects of the health systems of various geographic areas of the world. To date, these areas have included the Soviet Union, the People's Republic of China and others. In the future, these studies will probably be extended to include studies of health systems in other parts of the world.

Specifically, the objectives of the Fogarty International Center, in launching the Geographic Health Studies, were:

1. to advance the knowledge of American biomedical scientists, clinicians and health administrators of medical activities and systems in certain geographic areas of the world;
2. to publish selected documents concerning various phases of medicine and health programs in other countries; and
3. to improve cooperation among clinicians, health scientists and health administrators in the United States and other countries of the world.

In pursuit of these objectives, the Geographic Health Studies have focused on the following areas:

1. Research: including the general philosophy and organization of research, research trends and priorities, objectives, resources available and relationship to medical care;
2. Education and Training: including the education of both professional and sub-professional health manpower, the role of the medical school, the effect of health care requirements upon medical education, financing of medical education and the influence of public and private organizations upon medical school curricula;

3. Services: involving the organization of health services, respective rolls of public and private sectors in providing health services, the economics of health care, special services to population groups such as maternal and child care, geriatrics, mental health care, and the role of the medical school in providing health services.

During FY 1973 several publications were prepared within the aegis of the Fogarty Center's Geographic Health studies. These included:

1. Nutrition Research in the USSR, 1961 - 1970

This monograph is based on original Soviet research published within the past decade and was selected for publication by the Fogarty Center because of the considerable importance of nutrition in the United States as well as the emphasis placed upon it by the Soviet Government. Under the general category of nutrition, the Soviets include a number of areas that are not strictly classified as nutrition in the West. Thus, included in the Soviet nutrition studies are food technology, food toxicology, chemical composition of food and the role of food dyes in the etiology. Rather than distracting the Western nutritionist, however, the inclusion of peripheral scientific areas adds valuable concrete information for the reader. Then too, the Western nutritional scientist will also discover in this volume that a significant portion of Soviet nutritional research is directed toward elevating the nutritional status of industrial workers, an important goal of the Soviet Five Year Plans which delineate the quantity of all Soviet Research including that in the field of nutrition. Nevertheless, Western scientists reading this volume will find that by and large the general research directions and efforts in the field of Soviet nutrition are not substantially dissimilar to Western nutritional research. This volume, accordingly, provides the American nutritionist with a very useful tool with which to measure the level of his own nutrition research program.

2. Topics of Study Interest in Chinese Medicine and Public Health: Report of a Planning Meeting

This publication is a summary of an informal planning meeting concerning possible topics of scholarly interest in Chinese medicine. This meeting was convened at the Fogarty International Center, NIH, in Bethesda, Maryland on March 15, 1972, for the purpose of undertaking an exchange of ideas among biomedical and social scientists with a knowledge of the People's Republic of China to ascertain areas of Chinese medicine and public health which the Fogarty Center, through its Geographic Health Studies, could profitably pursue and derive therefrom useful publications. The report comprises ten themes covering such areas of Chinese biomedicine and public health as geographic pathology, traditional medicine, medical care in urban and rural areas, nutrition, medical education and others of specified interest.

The views expressed in this report represent those of the individual commentators and not necessarily those of any agency or part of the United States Government. Inasmuch as these opinions are only of an informal nature, this report was produced in limited quantities, primarily for those with a scholarly interest in medicine and public health in the People's Republic of China.

3. A Bibliography of Chinese Sources on Medicine and Public Health in the People's Republic of China: 1960 - 1970

In an effort to provide interested physicians, biomedical and health scientists in the United States with current information on medicine and public health in the People's Republic of China, the Fogarty International Center, in conjunction with the Library of Congress, has published this bibliography. It includes the numerous Chinese publications available in the United States on medicine and public health and covers primarily those Chinese sources published between 1960 and 1970, translated by the Joint Publications Research Service, and available at the Library of Congress and the National Library of Medicine. The bibliography, it is hoped, will help substantiate the scope and sophistication of China's health practices and interests which several American physicians recently returning from visits to China have articulated in various newspaper and magazine articles. The individual health professional should find much that complements his particular interests and work in this publication.

4. Medicine and Public Health in the People's Republic of China

In FY 1972 the Fogarty Center, in an effort to expedite the publication of recently completed essays on important aspects of biomedicine in China, published a paperback edition of "Medicine and Public Health in the People's Republic of China," comprising these essays by scientists of various disciplines with current backgrounds in China biomedicine. The demand for this anthology indicated that a second edition would be required. Accordingly, in FY 1973 the Fogarty Center published a newly edited hard-back edition of this anthology.

Among the essays included in this anthology are discussions on health care and the organization of health services in China, medical personnel and their training, population dynamics, pharmacology, nutrition and acupuncture. Generally, therefore, this document provides a highly useful summary and analysis of past and current biomedical activities in mainland China, especially apropos for those persons with a general interest in the subject of Chinese medicine. Beyond this, the study must also hold considerable interest for physicians, scientists, and health and science administrators concerned with expanding and improving the health care available to the American people.

K. OTHER ACTIVITIES OF THE FOGARTY INTERNATIONAL CENTER DESIGNED TO PROMOTE FURTHER INTERNATIONAL BIOMEDICAL COOPERATION AND PROJECTED STUDIES

In FY 1972 through meetings, correspondence and conferences, efforts were made to expand U.S. - Soviet biomedical cooperation, both through formal bilateral arrangements as recorded above and by means of less formal but productive associations. Steps were also taken to expand American knowledge of biomedical activities in the People's Republic of China. In FY 1973 these activities were continued. The commentary below reflects on the nature and success of these activities.

1. Soviet Health Studies

During FY 1972 a special opportunity to promote U.S.-Soviet biomedical cooperation arose in connection with the President's visit to Moscow in May 1972, at which time the U.S.-U.S.S.R. Agreement on Health Cooperation was formally signed. As was recorded above under the bilateral discussions, a binational committee (Joint U.S.-Soviet Committee for Health Cooperation) was created to initiate joint policies, evaluate progress and maintain general supervision through annual meetings, the first of which was held in Moscow in March, 1972.

At the Joint Committee's second meeting in March 1973, in Washington, significant progress was achieved in articulating further the principles of U.S.-Soviet cooperation and determining the practical methods through which this cooperation would be achieved. As in FY 1972, the Fogarty Center staff, through regular correspondence and consultation, developed a proposal for expanded cooperation which was presented to the Joint Committee for its consideration. After extensive discussions a Memorandum of Agreement with several protocols was signed by Dr. R. O. Egeberg, Co-Chairman of the Committee and Special Assistant to the Secretary of Health, Education, and Welfare for Health Policy and Dr. D. D. Venediktov, Co-Chairman and Deputy Minister of Health, Ministry of Health of the U.S.S.R.

The Memorandum of Agreement included provisions for a study of the Medical Theory and its Application in the Administration and Management of the Total Soviet Health System. This cooperation has been designed to apply to the total health system of both countries in that it encourages significant research on those health problems which are most debilitating to the American and Russian people and the solution of which would clearly improve the quality of health care in the two countries. The agreement specified those areas of cooperation which are delineated in the prior discussion on bilateral cooperation and established as an objective an exchange quota of 60 man-months for 1973-1974. The memorandum also specified the financial conditions under which this exchange would be conducted.

An important feature of this memorandum was the attached protocols identifying the specific problem areas in which cooperation was to be carried forth. These protocols identified the scientists and institutions involved in the cooperative area as well as establishing a plan of work for each area covering 1973 and 1974. The areas of cooperation for which protocols were addended include: cancer chemotherapy, ischemic heart disease, congential heart disease, leukemia and tumor viruses of animal and man, environmental health research, tumor cell genetics, cardiovascular disease and myocardial metabolism and pathogenesis of arteriosclerosis.

2. Chinese Health Studies

In FY 1973 the staff of the Fogarty International Center assisted the Director of the NIH in preparing for and welcoming two groups of representatives from the People's Republic of China. One group consisted of Chinese physicians and biomedical scientists who visited the NIH in October 1972 and the other comprised Chinese journalists who arrived at the NIH at the end of May 1973.

a. Visit of Chinese Biomedical Scientists and Physicians to NIH

On October 13 and 14 ten physicians and biomedical scientists from the People's Republic of China visited the NIH. This delegation, which was the first biomedical group to visit the U.S. from mainland China since the early 1950's, was the guest of the Institute of Medicine and the American Medical Association. The leader of this Chinese group was Dr. Wu Wei-jan, Vice-Chairman of the Association of Surgery, the All-China Medical Association, and the group included an obstetrician, gynecologist, surgeons, research scientists and a tuberculosis specialist as well as practitioners of traditional Chinese medicine.

While at the NIH the group was briefed by scientists from the NCI, NHLI and the staff of the Fogarty International Center. The briefing and discussions with members of the Chinese delegation were of particular interest and value to the Center. The Chinese were informed of the Center's China health studies, presented with copies of the Center's China publications and informed of the topics of special interest in Chinese medicine under consideration by the Center for the NIH.

b. Visit of Journalists form the PRC

A delegation of 21 newspaper executives and journalists from the People's Republic of China, on a six city tour of the United States, visited the NIH on May 30, 1973. The delegation was greeted both by Dr. Charles C. Edwards, HEW Assistant Secretary for Health and Dr. Robert H. Stone, Director, NIH. Dr. Milo D. Leavitt, Jr., Director, Fogarty International Center, presented the delegation with a briefing on the work of the Center with special emphasis on the Center's Chinese

Health Studies. The journalists, like the Chinese physicians and scientists, expressed a lively interest in the Center's Chinese program.

3. Visit of Dr. Marian Sliwinski, Minister of Health and Social Welfare, People's Republic of Poland

On the occasion of the visit of Dr. Marian Sliwinski to Washington in March 1973, at which time a Memorandum of Understanding for Cooperation in the Health Sciences was signed between the U.S. and Poland, Dr. Sliwinski visited the NIH including Fogarty International Center. During the course of the visit Dr. Sliwinski was informed of NIH programs with special emphasis on the cooperative U.S.-Polish health studies undertaken through the auspices of the PL-480 program (see previous discussion on PL-480, Section F).

4. Delegation to the WHO meeting in Geneva

Dr. Milo D. Leavitt, Jr., Director, Fogarty International Center, was selected as an advisor to the U.S. delegation of the twenty-sixth World Health Assembly meeting held in Geneva, May 5-25, 1973. Dr. Leavitt also attended the Governing Council meeting of the International Agency for Research on Cancer, May 3-4, 1973 as an observer for the NIH/DHEW. Dr. Leavitt was afforded the opportunity to discuss a number of areas of interest to the NIH, especially the WHO role in health care, while attending these meetings.

L. THE FOGARTY INTERNATIONAL CENTER: COORDINATING ROLE FOR NIH INTERNATIONAL ACTIVITIES

For a number of years the NIH has sought to employ the scientific productivity of foreign scientists in fulfilling its mission of improving the health and welfare of the people of the United States and in contributing to the base of scientific knowledge upon which American scientists depend. The continuing limitations on funding, of course, have accentuated the NIH intent to utilize outstanding resource opportunities regardless of geographic location. Several different mechanisms are used to obtain maximum benefit from these international resources, including foreign grants, publication of biomedical data derived from reports from abroad and information from NIH participants in international scientific conferences and symposia. Thus, in addition to its other programs discussed above, the Fogarty International Center performs a coordinating role in making available for the use of the NIH scientific community biomedical data derived through the aforementioned mechanisms.

1. Review of Foreign Grant Applications

In April 1968 the NIH expanded its review procedure for foreign grant applications to assure that each application for funding was of the highest scientific merit and was relevant to the program interest of the NIH. The Fogarty International Center was given the responsibility for reviewing all foreign grant applications for conformance with NIH, PHS, DHEW and other Executive Branch policies.

2. Administration of Foreign Travel Ceilings

The Fogarty Center was assigned the responsibility of administering the foreign travel ceilings for extramural activities of the NIH. Included in this responsibility is the development of ceilings, maintenance, allocation and reporting of these ceilings.

II

INTERNATIONAL COOPERATION IN THE HEALTH SCIENCES BY INSTITUTES, DIVISIONS AND OTHER COMPONENTS OF THE NIH

In addition to the activities in the international health sciences coordinated by the Fogarty International Center delineated above, many other components of the NIH participate in international programs, projects and activities designed to promote the biomedical sciences. These include cooperation with national and international organizations throughout the world. The following summaries of the more important aspects of these cooperative efforts afford some measure of insight into these activities.

A. THE NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

1. Nutrition

The National Institute of Child Health and Human Development (NICHD) is carrying out two studies in cooperation with the Institute for Nutrition in Central America and Panama and the Pan American Health Organization. One of these, using money allocated from the U.S.-Japan Cooperative Medical Science Program Funds, is the analysis and publication of data from a longitudinal study of nutrition, infection, and growth among pregnant and lactating women, infants, and young children in a small native village in Guatemala.

The second of these joint studies is a contract study being conducted in four villages in Guatemala. Begun in 1964, the investigation has given evidence that the adverse effects of poor maternal nutrition on the birth weight of the baby can be partially counteracted by caloric supplementation during pregnancy. This finding is of importance because low birth weight is a prime factor in infant mortality. In addition, since maternal height and weight at conception have also been found to influence birth weight, the study has made clear that efforts to improve nutrition must begin in the mother's childhood if she is to bear the healthiest children possible.

2. Contraception

Through its Center for Population Research (CPR) the NICHD has also negotiated several important contracts with institutions outside the U.S. In keeping with its continuing efforts to develop a variety of safe, efficacious contraceptive agents, the CPR supports a study at Loral University, Montreal, Canada, to synthesize analogs of chemical contraceptive drugs.

Under a contract from the CPR, scientists at the Karolinsky Institute, Stockholm, Sweden, are developing an "International Documentation Center"

in the biological and medical fields relevant to human reproduction. Journal articles, technical reports, monographs, and symposia will be included in the information gathering process.

As part of its program to evaluate the long-term effects of vasectomy, the CPR has contracted with the Netherlands Cancer Institute to study blood sera of naturally infertile men. Autoantibodies to sperm will be isolated from the sera and classified according to immunologic groups. These groups will then be examined to determine their association with various types of infertility. This study should lead to significant improvement in assay techniques used for studying antibodies and cellular immunity to sperm following vasectomy.

Dr. Merril S. Read, NICHD, presented a paper before the International Symposium on Malnutrition and Function of Blood Cells in Kyoto, Japan, November 27-30, 1972. At this symposium, sponsored by the Joint Malnutrition Panel, U.S.-Japan Cooperative Medical Science Program, Dr. Read spoke on the possible impact of anemia -- the most widespread nutritional deficiency in the U.S. -- on intellectual and behavorial development.

3. Remedial Learning

Supported by a grant from the NICHD, a team of investigators in Israel has developed a program of remedial learning techniques geared to the educationally retarded, culturally disadvantaged adolescent. It is hoped that these techniques, known as "instrumental enrichment", will produce significant changes in the learning process and improve the social integration, self-acceptance, and level of functioning of retarded adolescent youths at a point in their development when such changes or reversals are usually considered unlikely.

A group of 521 adolescents are being studied; one-half of the youths receive "instrumental enrichment", and the remainder receive "general enrichment". Preliminary results are encouraging and the investigator will determine the effectiveness of"instrumental enrichment" by follow-up studies of the youths as they move into new settings. These techniques have been taught to many educators in Israel and have been translated into English. It appears most likely that "instrumental enrichment" could be applied in many situations in the United States.

B. THE NATIONAL CANCER INSTITUTE

The basic understanding that cancer is a health problem that knows no boundaries is reflected in the National Cancer Act of 1971. The Act, which created that National Cancer Program, expressly requires international exchange and collaboration in the effort to fight cancer.

Specifically mandated by the National Cancer Act is the creation of an International Cancer Research Data Bank to collect, catalog, store, and

disseminate the results of cancer research undertaken in any country for the use of any person involved in cancer research in any country. Direct support of both American and foreign cancer investigators is also provided for. This can be accomplished through funding highly qualified foreign nationals, funding collaborative research involving American and foreign participants, or funding American scientists abroad and foreign scientists in the United States. These provisions underscore and implement a long recognized need to work on the cancer problem jointly with the world community of biomedical scientists.

In the months of FY 1973, accordingly, international activities have grown more prominent at the National Cancer Institute (NCI). A new Office of International Affairs headed by an Associate Director was created to assist, in cooperation with the Fogarty International Center, in managing the international component of the NCI's programs. The signing in May 1972 of a joint health agreement between the United States and the Soviet Union, which is discussed in detail in Part I of this report, resulted in several exchange visits of scientists and clinicians, as well as reciprocal shipments of viral materials and investigational drugs. Significant new international efforts in laboratory, clinical and field research were initiated in FY 1973, together with major programs in information exchange. These activities added to the ongoing foreign projects bring the NCI into contact with leading cancer research investigators and institutions throughout the world.

1. International Activities of the Office of the Director

The specific international activities and programs that have been pursued during FY 73 include the establishment of the Office of International Affairs, the Soviet exchange agreements, and the International Cancer Research Data Bank. Additional programmatic activities fall directly within the purview of the four NCI operating Divisions: the Division of Cancer Biology and Diagnosis, the Division of Cancer Cause and Prevention, the Division of Cancer Treatment and the Division of Cancer Resources and Centers. International cooperative activities involving these offices and divisions are described in the following sections.

a. Office of International Affairs (OIA)

The Office of International Affairs was recently created to plan, coordinate, and manage cooperative international cancer research activities and to provide leadership within the National Cancer Institute for the development of international programs and activities leading to the ultimate conquest of cancer.

As the research areas for the National Cancer Program develop and expand, it becomes increasingly necessary for the Institute to be involved in scientific problems which transcend national boundaries, and for the Institute to both foster and utilize the cancer expertise that exists

outside the United States. Through the Office of International Affairs the NCI will act to carry out these international objectives.

The OIA is to be the focal point for all NCI activities abroad including those efforts within the National Institutes of Health relating to international cancer research. Within the NCI, the Associate Director for International Affairs is providing leadership and assistance to other NCI components in the development, planning, coordination, implementation, and effective management of international programs and activities.

The Associate Director for International Affairs is actively pursuing cooperative links between the NCI research programs and parallel international programs. He is working on behalf of the NCI for effective coordination of cancer research among three major international organizations: The World Health Organization (WHO -- Cancer Unit), the International Agency for Research on Cancer (IARC), and the International Union Against Cancer (UICC). These organizations are important resources in terms of membership and experience, and are appropriate mechanisms for international operations. The National Cancer Institute's support to and close collaboration with these organizations is essential; efforts to this end have been vigorously pursued during the past year. Developing and maintaining liaisons with the Fogarty International Center, other NIH components, Federal departments and agencies are equally important responsibilities of the Office of International Affairs. Throughout all these activities, the overriding goal is to maximize the opportunities for further insight and understanding of the nature of cancer so that the incidence, morbidity, and mortality of cancer in man can be reduced.

b. International Cancer Research Data Bank (ICRDB)

The National Cancer Act of 1971 required the NCI to establish an International Cancer Research Data Bank for the purpose of making cancer research information available to investigators working in any country. This mandate included collecting, cataloging, sorting, and disseminating the results of cancer research undertaken throughout the world. With the assistance of several international advisors, the NCI has sought to clarify its responsibilities for this activity.

In May 1972, an international planning meeting was attended by twenty-six participants from seven countries. The group concluded that the NCI could not feasibly nor financially establish a repository for all the world's cancer literature; instead, support should be rendered to various projects meeting specifically defined information needs.

In the planning and developments for the ICRDB pursued in FY 1973, scientists and information specialists from institutions or organizations in Canada, England, France, Germany, Switzerland, the Netherlands, Belgium, Hungary, and the Soviet Union have met with the NCI staff to plan mutual information exchange programs. The staff have also consulted with the UICC, the IARC,

the WHO, and the European Organization for Research on the Treatment of Cancer (EORTC) for planning and program guidance.

An International Advisory Committee for the ICRDB is being organized to review projects proposed for funding, and to assist in the establishment of information exchange systems and mechanisms. The committee will be under the auspices of the UICC and will be financed by the NCI. Both the U.S. Department of State and the DHEW Office of International Health have cooperated in establishing the committee.

One of the first activities to be supported as an ICRDB service is the newly created Registry of Tumor Immunotherapy. Clinical investigators researching means to treat cancer by stimulating the body's own immune defense mechanisms are being invited voluntarily to submit to the Registry copies of their current protocols, results of clinical trials and selected patient data. The rapid and accurate exchange of information about this research activity is one of the Registry's prime purposes. One issue of a Registry newsletter has already been published, and a second is in press. Over two dozen protocols have been received in the first months of operation from clinicians in the United States, Canada, England, Sweden, Switzerland, Yugoslavia, and the Soviet Union. The participation is expected to expand to include several other countries as well.

c. U.S.-U.S.S.R. Health Exchange Activities

As was recorded in Part I, in March 1972, at the first session of the U.S. - U.S.S.R. Joint Committee for Health Cooperation convened in Moscow, one of the areas agreed upon for bilateral effort was malignant neoplasms. It was agreed that the work would focus initially on four central cancer problems: cancer chemotherapy; immunotherapy of human tumors; leukemia and tumor viruses in animals and man; and genetics of tumor cells.

During FY 1973, at the second session of the Joint Committee, plans were expanded and a series of joint protocols formulated. In FY 1973 a significant level of exchange activities was conducted in both countries. Four Soviet delegations visited the United States, touring the laboratory and clinical facilities at the NIH and at universities and research institutions across the country. Thirty-five U.S. scientists on seven separate missions have been to Moscow.

As a result of the discussions and planning conducted in these visits, a number of chemical compounds, viruses, and cell cultures have been exchanged. A cell separator unit was sent to the Institute of Experimental and Clinical Oncology in Moscow. Joint research projects are being carried out in virology, and cooperative clinical trials for chemotherapy have begun. A joint publication on drug development and screening methodology is planned, together with an international conference on the same topic. Additional agreement in the areas of epidemiology, cancer centers, and

cancer control are being explored for more cooperative programs. The progress to date demonstrates that significant cooperation is possible and that the fight against cancer can be advanced by this international collaboration.

2. International Programs of the Operation Division

In the following four sections, the international activities of the NCI's operating Divisions are briefly discussed. The projects conducted in foreign countries represent unique capabilities -- special expertise, facilities, and population -- which can contribute to the accomplishment of various NCI research programs. In pursuing grants, contracts, and agreements outside the United States, the NCI seeks to increase communications among the worldwide scientific community committed to cancer research and to maximize the opportunities for important new knowledge.

a. Division of Cancer Biology and Diagnosis

The primary research activities of this Division which are conducted abroad are contracts in immunology, immunobiology, immunodiagnosis and immunotherapy. The participating institutions include the Weizmann Institute of Science and Tel Aviv University in Israel, the Karolinska Institute in Sweden and the Walter and Aliza Hall Institute of Medical Research in Australia. The Breast Cancer Task Force also has several contracts with foreign institutions; the research covers investigations from animal mammary viruses to steroid excretions to epidemiologic patterns in special populations. The International Agency for Research on Cancer, the State University of Utrecht, the Austrian Academy of Science's Institute for Molecular Biology and the Hebrew University Hadassah Medical School are some of the organizations working with the NCI in this area.

In the Laboratory of Pathology and its component sections, NCI staff have pursued collaborative studies on comparative morphology and staging for a variety of different cancers. Work with the Atomic Bomb Casualty Commission in Japan and the Lymphoma and Solid Tumor Treatment Centers in Uganda has been part of their programs.

b. Division of Cancer Cause and Prevention

The Division of Cancer Cause and Prevention covers three important areas of cancer research: biometry and epidemiology, chemical carcinogenesis, and virology. Each of these program areas relies upon the international scientific community for research capabilities and unique resources.

The Biometry and Epidemiology Branches are investigating cancer in different populations throughout the world. Work continues on migrant studies of Japanese persons who have emigrated to Hawaii and to California;

and on Norwegian and Polish populations in those countries and in the United States. Pediatric cancers have been highlighted in international collaborative work and at a conference co-sponsored with the IARC, WHO and the International Society of Pediatric Oncology. The Manchester (England) Childhood Tumor Registry has provided a unique opportunity to study the etiology and therapy of childhood cancers. Research efforts with the Atomic Bomb Casualty Commission continues along with the International Commission on Radiological Protection to discover the effects of radiation on cancer. The collaboration with the Atomic Bomb Casualty Commission has paid off in a modified Japanese attitude toward the ABCC, so that there is now substantial involvement of several Japanese universities, including the development of a tissue registry at Hiroshima.

The Chemical carcinogenesis program relies upon the IARC in its mission to screen natural and man-made environmental substances for carcinogenic activity. It has contracts with the IARC to produce monographs on carcinogenic agents, and the Program supports collaborative conferences by the IARC.

In the Viral Oncology area, NCI scientists are exploring a variety of studies on animal and candidate human viruses. The collaborative research has involved investigators at the Karolinska Institute and University of Upsalla in Sweden, the University of Denmark, the Max Planck Institut fuer Virusforschung in Germany, the Netherland Cancer Institute, Hebrew University in Israel, and the Cancer Institute in Tokyo, Japan. Additionally, contract work has been conducted by the IARC, the Tel Aviv University and Weizmann Institute in Israel, the Universities of Naples and Padua in Italy, the Makerere University in Uganda, and the Aichi Cancer Center in Japan.

c. Division of Cancer Treatment

The Division of Cancer Treatment is responsible for a comprehensive drug development and drug screening program which covers all aspects from testing substances for anti-cancer potential to their purification and testing in animals to their formulation and clinical trial in human patients. As such, the Division maintains close relationships with worldwide cancer chemotherapy programs with a view to (a) information exchange pertaining to latest scientific developments in chemotherapy, (b) opening new avenues for procurement of synthetic agents and natural products for screening, and (c) identification of new compounds of potential interest for chemotherapy.

d. Division of Cancer Research Resources and Center

The international programs and projects of the Division of Cancer Research Resources and Centers focus upon cooperative clinical trials. These trials are highly precise testing of certain chemotherapeutic agents and regimens upon select patient populations so that a scientific evaluation can be made as to the efficacy of one method for treating a

type of cancer versus another method. Together with the Division of Cancer Treatment, the Division of Cancer Research Resources and Centers supports liaison activities between clinical cooperative groups in the United States and in Europe. The primary liaison mechanisms are the EORTC and the Committee on Controlled Therapeutic Trials of the UICC. Grant monies have enabled exchange visits, planning meetings and extensive documentation.

Close liaison is being maintained with investigators in leading institutions abroad, including universities, medical schools and pharmaceutical houses. Active contacts continue to be maintained through the IARC, the EORTC, and the Chemotherapy Committee of the UICC.

The Division of Cancer Treatment has appointed a liaison representative to the Cancer Institute in Tokyo, Japan and at the Institut Jules Bordet in Brussels, Belgium. These representatives provide a mechanism for close collaboration encompassing both the preclinical and clinical cancer chemotherapy programs of Asia and Europe with that of the NCI. They are increasing the input into the chemotherapy screening program at the NCI and fostering collaboration in the study of new anti-cancer drugs. These representatives enable not only contact with universities, medical schools, the chemical industry, and pharmaceutical houses in the various countries, but also enable the continuous review, abstracting, and translating of significant foreign reports.

During FY 1973, the Division staff have participated in a variety of conferences and symposia throughout the world including Europe, Africa, the Soviet Union, India, Australia, and New Zealand. Their expertise in drug development and clinical trials has led to significant international activity for program development in other countries.

C. THE NATIONAL HEART AND LUNG INSTITUTE

1. Cardiovascular Diseases

In Part I, Section I, Bilateral Agreements, we observed that one of the three principal areas of U.S.-Soviet biomedical cooperation is cardiovascular diseases. The following represents a detailed summary of the NHLI, including discussions of the more important aspects of the problems of cardiovascular treatment, the dimensions of the proposed bilateral cooperation and the visitors and meetings involved in implementing this cooperation.

At the first meeting of the U.S.-Soviet biomedical cooperation is cardio-Cooperation held on March 27-31, 1972, it was agreed that "both parties will develop mutual cooperation in the fields of health and medical science which are of greatest significance, firstly the problems of cardiovascular diseases..." As a result of the meetings of the Working Groups under the U.S.-.U.S.S.R. Joint Committee for Health Cooperation both parties outlined specific problems and forms for cooperation in each designated area including cardiovascular disease.

This cooperative effort was further articulated in the May 23, 1972 five-year agreement between the United States and the Soviet Union on Cooperation in the Field of Medical Science and Public Health. The Agreement specified that "By mutual agreement and on the basis of reciprocity, they will determine the various directions of this cooperation, proceedings from the experience acquired by the Parties in the course of previous contracts, visits, and exchanges".

The important element in this agreement which did not exist in the earlier cooperative programs is the mutual planning and execution of joint research activities according to an organized work plan. The earlier exchanges of delegations were for relatively brief visits, usually for about three weeks, touring various medical institutions in the specialized field previously agreed upon for the exchange. Under the new agreement Annual Progress Reports and proposed plans for the total cardiovascular program are to be submitted to the Joint Committee for their consideration.

Dr. Theodore Cooper, Director, National Heart and Lung Institute, is the overall coordinator for the United States of the cardiovascular studies to be conducted under the agreement. Coordinators for the U.S.S.R. are Deputy Minister of Health, Dr. Eugene I. Chazov and Professor Igor Shkhvatsabaya, Director of the Myasnikov Institute.

a. Topics of Initial Collaboration - Cardiovascular Area

At its first meeting in 1972, the U.S. - U.S.S.R. Joint Committee selected four programs for initial collaborative efforts in cardiovascular diseases:

1) Pathogenesis of Arteriosclerosis
2) Management of Ischemic Heart Disease
3) Myocardial Metabolism, and
4) Congenital Heart Disease

Arteriosclerosis is the most common type of cardiovascular disease and is the chief cause of death in the United States and the U.S.S.R. Ischemic heart disease is the most common clinical complication of arteriosclerosis and the most common complication leading to death. Myocardial metabolism is a topic involving the study of the activities and functions of the healthy and diseased heart and is thus a topic of relevance for all types of heart disease. Congenital heart disease is an important disease of children in both countries and is of particular interest to cardiovascular surgeons who have devised ingenious techniques for the successful repair of most congenital heart defects at an early age.

The first two of the joint programs involve detailed clinical studies of large numbers of patients, the third consists primarily of studies seeking new basic information which can be used in the prevention and treatment of disease, and the last project is a study of improved

surgical techniques and better life-support systems for open-heart surgery in children as well as improved methods for detecting and evaluating congenital heart defects.

The Committee also decided to initiate contacts and exchange of information in the area of mechanical circulatory assistance. Exploratory activities in microcirculation, cardiogenic shock, sudden death, thrombolytic treatment of myocardial infarction, and hypertension were also authorized.

b. Progress During the Past Year

Substantial progress has been achieved in all four programs during the past year.

Problem 1. Pathogenesis of Arteriosclerosis

Subject 1. The prevalence of hyperlipidemias and ischemic heart disease in the populations of the U.S. and U.S.S.R.

This is the first study of its kind in the world. It will involve large numbers of well characterized subjects in two countries, comprehensively studied according to identical techniques based on carefully worked out research protocols, and analyzed by highly standardized techniques. The goal is to compare the prevalence of hyperlipidemia and ischemic heart disease in populations from the U.S. and U.S.S.R. The study will seek to determine, over a period of several years, whether modifications of blood lipids by diet or drugs will diminish the risk of ischemic heart disease.

Accomplishments during the past year include exchange of information, exchange of health professionals, and elaboration and agreement on a plan for the study.

A 350-page highly technical document describing details of the organization, protocols, procedures and data management developed and tested in the NHLI Lipid Clinics was translated into Russian by the Fogarty International Center at the request of NHLI during the fall of 1972 for transmittal to U.S.S.R. scientists upon their arrival in the U.S.A. Professor A. N. Klimov of Leningrad and H. N. Gerasimova of Moscow examined the U.S. operation in detail. They visited American clinics and laboratories during the first scientific exchange in November 1972 through January 1973, and participated in the joint development of a preliminary plan for the study. Further agreement on the plan was reached during a visit to the U.S.S.R. from March 17 to 25, 1973 by Drs. Frederickson, Levy, Grizzle, Tyroler and Nichols of the U.S.A.

It has been agreed that the combined U.S.-U.S.S.R. study will be of men, aged 40-59 years. On the U.S. side, the Lipid Clinic Program expects to study approximately 22,000 subjects in Phase 1 and from 3,000 to 5,000

in Phase 2. The National Heart and Lung Institute has agreed to make available two Technicon Autoanalyzers to the U.S.S.R. for use in the combined project, subject to provision of maintenance and reagents by the U.S.S.R.

Problem 2. Management of Ischemic Heart Disease

Subject 1. Comparative study of differential approaches for medical and surgical treatment of ischemic heart disease

This project is also the first of its kind. It aims, over a period of years, to evaluate and compare chronic angina and heart attack disability treatment methods that have been developed in each country up to the present. The collaborative study planned in this area will be a systematic assessment of the way well-defined patients are treated in both countries.

Accomplishments during the past year include exchange of information, exchange of health professionals, elaboration of criteria for selection of patients for differential medical and surgical treatment and elaboration of work plans for joint studies.

Discussions regarding the criteria for selection of patients and agreement upon criteria for assessment of effectiveness of treatment were begun during the visit by U.S. scientists to the U.S.S.R., September 15 - October 1, 1972. The U.S. team consisted of Drs. Frommer, Cornfield, Reeves, and Willman, During this visit, detailed methodological plans were developed for a collaborative study of the management of severe chronic angina pectoris by "differential" intensive medical management in the U.S.S.R. and by aorta-coronary bypass surgery in the U.S., with the addition of a reference group of "conventional" standardized medical regimens, alike in both countries. Detailed draft protocols were exchanged on schedule by December 31, 1972. These protocols were then translated in preparation for the February 6-9 meeting in Bethesda of U.S. and U.S.S.R. scientists. The U.S.S.R. participants were Drs. Shkhvatsabaya, Dolapchyan, Grigoryants, Mzur and Shvetsova. A second joint draft protocol was developed during the meeting for the purpose of planning feasibility studies and ultimate implementation.

Agreement has been reached on most of the difficult methodological tasks of the study such as characteristics of the reference group; details of the standardized therapy of the reference group; end points for the reference group; and follow-up protocol for the study groups, including repeat angiography and repeat exercise tests. The techniques for coronary angiography and ventriculography have been examined in great detail and agreed upon by the two sides. A grading system for interpreting the the results has been developed and means of achieving standardization of interpretation have been agreed upon.

Revisions of the data sheets were made consistent with the new protocols and forwarded to the U.S.S.R. Coordinator on May 15, 1973.

Problem 3. Myocardial Metabolism

The role that this basic research project on the study of myocardial metabolism will play in the future overall development of cardiovascular programs is likely to be a very important one in terms of joint development of both therapy and prevention.

Accomplishments during the past year include exchange of information, the arrangements for a symposium, and preparations for joint publication of the proceedings of the symposium.

The preliminary plans for the symposium were presented in a letter from Dr. Braunwald to Dr. Chazov on July 25, 1972. Dr. Chazov expressed his complete agreement with the agenda for the Symposium on Myocardial Metabolism and Function. A U.S. committee met on November 18, 1972, in Dallas, Texas, for the purpose of more detailed planning of the symposium. Final agreement on the details was reached during the February 26 through March 1 visit to the U.S.S.R. by Drs. Braunwald, Mayer, Morgan and Hegyli. The symposium will be held in Ponte Vedra Beach, Florida, November 4-6, 1973. One of the major objectives of this symposium is to improve scientific communication between our two nations and proceedings of the conference will be published as quickly as possible in both languages to ensure maximum dissemination of the results. Joint publication of the English version is scheduled as a Supplement to Circulation Research. This will be sent to all who subscribe to this journal (approximately 5,000 cardiovascular scientists) but it will also be reprinted as a separate monograph.

Problem 4. Congenital Heart Disease

Congenital heart defects are present in an estimated 50,000 of the children born in the U.S.A. each year and a corresponding number of children born in the U.S.S.R. Approximately 80 percent of these can now be cured or helped by surgery. The objectives of the collaborative study of congenital heart disease are to develop techniques of diagnosis and methods of post-operative care, to study the mechanisms of development of pulmonary hypertension, to search for new ways of reducing mortality from the surgical treatment of tetralogy of Fallot; and to study diagnostic techniques and surgical treatment of complex heart defects.

Accomplishments during the past year include exchange of information, exchange of health professionals, arrangement for a symposium and preparations for joint publication of the proceedings of the symposium.

Initial arrangements for the symposium were discussed in an exchange of letters between Drs. Gerbode and Burakovsky. A formal planning meeting

was held in Moscow, October 19-20, 1972. The symposium was held in Washington, D.C., April 9-11, 1973. The American Committee will publish the Symposium papers both in English and Russian. Each side assumed the responsibility for editorial review of its respective language.

c. Plans for the Future

Plans for the future include the agreement and implementation of the plans for the clinical studies in Problems 1 and 2, meetings to discuss the results of the pilot studies planned for the coming year, exchange of health professionals, and the exchange of technical data and results.

In Problems 3 and 4 the plan calls for the holding of symposia described above, the publication of the proceedings, the development of specific plans for further collaborative efforts on problems discussed at the symposia, the exchange of further information, and the exchange of health professionals.

The subject of mechanical circulatory assistance was explored during 1972 by Professor V. I. Shumakov during his visit to the U.S., September 24 to October 26 and by Drs. Dennis, Harmison, and Rakita during their visit to the U.S.S.R., February 23 to March 5, 1973. These contacts will be developed further during the coming year for the purpose of arriving at a specific plan of collaboration.

Plans have been completed for translations of U.S.S.R. abstracts to be published periodically in Circulation as special supplements. The first supplement will be published as soon as the abstracts are received from the Soviet side.

Arrangements have also been made with the editor of Cardiovascular Surgery for translation of U.S.S.R. abstracts and articles to be published in that journal upon editorial approval.

A review of current books in the cardiovascular area is underway for the purpose of identifying Soviet books which need to be translated for use by scientists engaged in the joint U.S.-U.S.S.R. program.

d. New Initiatives

A number of areas of potential mutual interest were discussed during the March 26-30 meeting of the Joint U.S.-U.S.S.R. Committee in Washington. The Committee agreed to the development of two new initiatives in the cardiovascular area:

Problem 5. Sudden death

Problem 6. Blood transfusion, blood components and prevention of hepatitis, with particular reference to cardiovascular surgery

Exchange of information, exchange of health professionals, and meetings between Soviet and American specialists will be held to develop plans for scientific cooperation in these areas during the coming year.

The American Committees in both Problem 5, Sudden Death, and Problem 6, Blood Transfusion, have held initial planning sessions and preliminary protocols have been developed for their upcoming October U.S.S.R. visit.

2. International Visitors and Meetings

The National Heart and Lung Institute's mission transcends national boundaries. During FY 1973 the NHLI received numerous international visitors. In addition, NHLI staff members have taken part in international meetings. A brief description of these activities follows.

In July 1972, Dr. Robert L. Ringler, Deputy Director for NHLI, had conversations with Dr. Ricardo Diez-Hochleitiner, Member of the Board, General Mediterranea, Madrid, Spain, concerning the exchange of scientific information between the United States and Spain. Dr. Diez-Hochleitiner discussed the establishment of a new institute for cardiovascular disease in Spain and possible future cooperation in the attack on cardiovascular disease.

On August 2, the Minister of Health of the U.S.S.R., Boris Petrovskv visited NIH with a delegation of eight Soviet health specialists. Dr. Ringler reviewed for the delegation the Cardiovascular Portion of the U.S. - U.S.S.R. Health Exchange Program, which at that time consisted of Problem Area 1 - Pathogenesis of Arteriosclerosis, Problem Area 2 - Management of Ischemic Heart Disease, Problem Area 3 - Myocardial Metabolism, Problem Area 4 - Congenital Heart Disease, and one Task-Mechanical Circulatory Assist. Dr. Donald Frederickson, Director for the Division of Intramural Research of NHLI and Dr. Andrew Morrow, Chief of the Surgery Branch of Intramural Research, discussed the Institute's intramural programs. These programs were of particular interest to Minister Petrovsky since he is a cardiovascular surgeon.

On August 29 and 30, NHLI hosted a symposium in Bethesda of the International Union of Nutritional Sciences, entitled "Hyperlipidemia in Relation to Cardiovascular Diseases and Diabetes". This symposium was coordinated by Dr. Gardner C. McMillan, Associate Director for Etiology of Arteriosclerosis and Hypertension, NHLI-DHVD. Topics discussed at this symposium were epidemiological, nutritional, and genetic considerations; insulin and lipemia; lipoprotein lipase; adipose tissue metabolism; metabolism of the vessel wall and nutritional control of lipid cholesterolemia.

On September 15, Dr. Theodore Cooper, Director, NHLI, met in Bethesda with Dr. Ricardo Diez-Hochleitiner, Mr. Fernando Larrain and Dr. Leopoldo M. Osorio, representatives of Fundacion General Mediterranea, Madrid,

to discuss plans for a future cardiovascular disease project under the direction of Dr. L. Osorio. These Spanish scientists also expressed a special interest in the provision of the Heart, Blood Vessel, Lung and Blood Act of 1972.

Dr. Cooper participated in the World Health Organization/International Society of Cardiology Symposium on Prevention of Ischemic Heart Disease (IHD): Metabolic Aspects and Other Specific Discussions in Madrid, Spain, October 2-4, 1972. The purpose of this meeting was to review the current status of studies on selected aspects of lipid, carbohydrate, nutritional and hormonal drug metabolism with a view toward: (1) assessing whether specific public health recommendations for preventing ischemic heart disease (IHD) are warranted; and (2) developing recommendations for new or additional studies which would be helpful in understanding the metabolic factors in the genesis or expression of IHD. Dr. Cooper monitored the session on Critical Review of Ongoing Trials on Prevention, during which he and Dr. Osorio again discussed possible NHLI support of cardiovascular research in Spain through Fundacion General Mediterranea. Dr. Cooper suggested that Osorio provide an overview of the Foundation's program and plans in preparation for support of a cardiovascular project in Spain. The discussions were cordial and ended on a positive note. Many participants in this international Symposium expressed great interest in the National Heart, Blood Vessel, Lung and Blood Act of 1972.

A presentation of the NHLI's programs in heart, lung, and blood research was made to a group of French journalists on October 3. They were particularly interested in the moral and ethical questions of life-support devices, such as the artificial heart, and the setting of research priorities. The French journalists were very well-informed on U.S. research programs.

An NHLI Symposium on Medical and Surgical Management of Coronary Artery Disease was held on October 14 as part of the program to familiarize eleven visiting Chinese scientists from the People's Republic of China with U.S. cardiovascular science. Dr. Robert Marston, former Director of NIH, and Dr. Theodore Cooper, Director, NHLI, welcomed them to the symposium. This was the first visit to NHLI by scientists from the People's Republic of China. Dr. Donald Frederickson, Director of NHLI's intramural programs, gave a presentation on "The Magnitude of the Problem of Artery Disease in the United States". Dr. Stephen Epstein, NHLI staff member, and Dr. Richard Gorlin, Associate Professor of Medicine, Peter Bent Brigham Hospital, Boston, gave a joint presentation on "The Anatomy, Natural History and Medical Management of Coronary Artery Disease". Dr. Frank Spencer, New York Medical Center, and Dr. Charles Hufnagel, Georgetown University, discussed "Myocardial Revascularization Through Surgery". Dr. D. Frederickson concluded the program with a presentation on "Prevention Rather Than Cure".

In November 1972, Dr. Claude Lenfant, Director for the Division of Lung Diseases, NHLI; Dr. Lowell Harmison of the Division of Technological

Applications, NHLI; and Dr. John Norman of the Texas Heart Institute, Houston, made a two-week visit to eight German research and development centers and the Ministry of Science and Education, Federal Republic of Germany. The purpose of the visit was to ascertain the status of German research in artificial circulatory support. The institutions visited were the Biotechnical Laboratory and AEG Telefunken, West Berlin; Technical University of Aachen/University of Duesseldorf; Siemens; Institute of Biomedical Techniques, University of Erlangen; Messerschmidt-Bolkow-Bloohm; Nuclear Research Center, Karlsruhe and Gesellschaft fuer Strahlen-und-Umweltforschung m.b.H. (GSF) Neuherberg (near Munich).

On November 22, 1972, Ms. Aveva Meyer of the Hebrew University of Jerusalem visited Dr. Gardner C. McMillan, Associate Director for Etiology of Arteriosclerosis and Hypertension, NHLI-DHVD, to discuss types of research areas being supported by the Atherogenesis Branch of NHLI.

On February 28, 1973, nine members of the 1973 Japanese Study Mission of the Council for Science and Technology visited Dr. Cooper and Dr. Frederickson for discussions on U.S. science and technology policies in the 1970's in relation to cardiovascular research so that a comparative analysis of the Japanese science and technology policies in the cardiovascular area could be made by the team.

On March 16, 1973, the Polish Minister for Health and Social Welfare, Dr. Marian Sliwinski, and a delegation of four Polish health specialists visited NHLI and had the opportunity to meet with Drs. Cooper, Frederickson and Morrow, as well as members of their staffs. Dr. Cooper summarized the NHLI organization, manpower, budget, programs, mechanisms of support of intramural as well as extramural research and generated lively discussions. Dr. Frederickson discussed current intramural programs in surgery, cardiology, endocrinology, experimental therapeutics, molecular disease, kidney and electrolyte metabolism, chemical pharmacology, chemistry, pulmonary diseases, and technical development. Dr. Morrow gave a brief review of some of the current trends in cardiovascular surgery, commented on coronary bypass surgery, and took the visitors on a tour of the acute coronary care unit, the automatic data processing facilities for the patients in this unit, and the cardiovascular surgical suites at the Clinical Center, NIH. In addition, one of Dr. Morrow's associates, Dr. Bruce Reitz, accompanied Minister Sliwinski, who is a cardiovascular surgeon, on his tour of cardiovascular surgical facilities at Baylor Medical Center and Stanford University.

During April 10-21, 1973, Dr. Michael Ashley-Miller, Senior Medical Officer, Division of Social Medicine of the Medical Research Council, London, England, visited NHLI as a consultant. He conducted several informal seminars on "Smoking," "Privacy and the Use of Medical Records for Research," "Cardiovascular Epidemiology and Clinical Trials," "The Rothshild and Dainton Reports," and the "Medical Research Council."

Mr. Reinhard Loosch, Deputy Assistant Secretary in Charge of International Cooperation, Federal Ministry of Research and Technology, Federal Republic of Germany, visited Dr. Robert Ringler on May 14. Dr. Ringler summarized the main areas of research supported by NHLI. Mr. Loosch, who is responsible for several bilateral scientific and technological arrangements between the Federal Republic of Germany and the United States, discussed areas of possible future collaborative research with the NHLI.

During June, NHLI staff made presentations to two groups of Soviet journalists. The first group was a delegation of six Soviet science writers: Mr. Jaroslav K. Golovanov of the Komsomolskaya Pravda, Mr. Mikhail Rebrov of the Krasnaya Zvezda, Mr. Oleg Kuprin, Deputy Chief Editor of the Znaniye-Sila, Mr. Bronislav Koltovoi, Science and Technical Editor of Izvestia, Mr. Lev Koshelev of the International Commission, Union of Journalists of the U.S.S.R., and Mr. Nikolai G. Shartse of the Tass News Agency. Dr. Ruth J. Hegyeli, Chief of the Program Development and Evaluation Branch, NHLI, briefly discussed NHLI's mission in the U.S. and to a greater extent the cardiovascular projects of the U.S. - U.S.S.R. Health Exchange Program. Later in June, two Soviet journalists, Mr. Vladimor Nikolaev, Deputy Editor-in-Chief of Ogonyok (a Soviet magazine similar to Life) and Mr. Demitriv Baltermants, a photographer for the same journal, who had accompanied Mr. Brezhnev to the United States, visited the NHLI to discuss the Institute's participation in the scientific exchange program between the U.S.S.R. and the U.S. The U.S. Coordinators for the seven joint cardiovascular research projects met with these journalists and discussed developments in each individual project area. The journalists were also given an opportunity to visit NHLI's cardiovascular surgical facilities and photographed an ongoing open heart operation.

During Mr. Brezhnev's U.S. visit, Dr. Chazov, Deputy Minister of Health of the U.S.S.R., who accompanied Mr. Brezhnev and who also is the U.S.S.R. Coordinator of the Cardiovascular Portion of the U.S. - U.S.S.R. Health Exchange Program, was guest at a luncheon held in his honor by Assistant Secretary for Health, Dr. Charles Edwards. Drs. Cooper and Ringler attended. At this luncheon, Dr. Chazov spoke in general of developing closer scientific relations between the U.S. and U.S.S.R.

Seventeen Japanese executives and physicians, sponsored by the Japan Productivity Center, visited the NHLI during June. They were particularly interested in programs to educate the public, since there is currently a rapid increase of cardiovascular disease in Japan. Dr. Cooper discussed in detail the NHLI's preventive and educational health care programs.

D. THE NATIONAL LIBRARY OF MEDICINE

The National Library of Medicine's international activities, which vary in scope, mechanism and immediate objective, all share the common criterion that they be of demonstrated value to the United States.

1. Acquisition and Document Exchange Program. The extensive acquisition and document exchange program of the Library continues, with 895 partners in 88 countries. The People's Republic of China, with its resumption of scientific publications in January 1973, is again included in this program. Under the AID Agreement, approximately 19,000 services were provided to 48 developing countries.

2. Special Foreign Currency Program. The Library's Special Foreign Currency Program supported 137 scientific projects in seven countries during FY 1973, 41 of which were new awards. This program, which aids in the dissemination and exchange of information important to the progress of medicine and public health through the use of foreign scientific personnel and resources, is funded by appropriations of blocked currencies. Sixty-nine projects were active in Israel in FY 1973 and forty-four in Poland under the Library's bloc grants in those countries. Included among these projects are the preparation of biomedical research and practice; the translation and publication of significant current and historical monographs in the biomedical sciences; publication of major international symposia and conference proceedings; indexing of foreign language literature for MEDLARS and MEDLINE; publication of authoritative bibliographies and other literature tools in special public health fields.

3. The MEDLARS Program. The eight bilateral agreements concerning MEDLARS with the United Kingdom, Sweden, France, Germany, Japan, Australia, Canada, and the World Health Organization, continue to function well. The bilateral mechanism and the quid pro quo character of these agreements are being looked upon by other agencies and organizations as a model kind of activity for international cooperation.

4. The MEDLINE and TOXLINE Projects. Topics currently under consideration relate to the future availability of the Library's on-line time-shared systems, MEDLINE and TOXLINE. Sweden has the MEDLINE data base under a special quid pro quo basis and is providing services to Scandinavia. Under an experimental arrangement, Institute National de la Sante et de la Recherche Medicale (INSERM) is using a Tymshare node in Paris to access the NLM computer for MEDLINE services. Plans are under way for the holding of detailed technical sessions on these matters with the Directors of the Foreign MEDLARS Centers. A second International MEDLARS Policy Meeting will be scheduled later in the year.

5. Cooperation with BIREME. Latin America has consistently been responsible for almost 58% of the requests NLM has received for services. NLM continues to provide technical consultation and backstopping to the Pan American Health Organization Regional Library of Medicine (BIREME) in Sao Paulo, Brazil. BIREME provides over 50,000 services within Brazil and will now increase its activities to other Latin countries. New activities being initiated include an extensive training program for users, managers, librarians, and technicians; an audiovisual program; and an experiment to operate the MEDLINE data base for the provision of bibliographic services.

6. Cooperation with the U.N. Specialized Agencies and Other International Organizations. NLM has varying degrees of involvement with a number of international organizations, both governmental and non-governmental, scientific and non-scientific in character. These include the United Nations;

the U.N. specialized agencies which have a health or scientific orientation such as the World Health Organization (WHO) and the United Nations Education, Scientific and Cultural Organization (UNESCO); economic organizations, such as the Organization for Economic Cooperation and Development (OECD); and scientific, such as the International Council of Scientific Unions (ICSU) Abstracting Board.

E. THE BUREAU OF HEALTH MANPOWER EDUCATION

During FY 1973 the Bureau of Health Manpower Education, NIH, engaged in a variety of international activities consistent with its responsibilities to administer those Federal programs which are concerned with improving the quality and increasing the supply, effectiveness and availability of health manpower resources within the United States. Particular concern is directed to the health professions (medicine and osteopathy, dentistry, pharmacy, optometry, podiatry and veterinary medicine), to professional nursing, and to the allied health professions.

Many nations, facing even more pressing problems of health manpower resources than our own as well as international assistance agencies, including WHO, turn to the Bureau for technical information and consultation. Such assistance is provided freely through correspondence, working papers, and conferences both within the U.S. and abroad. Of particular significance to the U.S. health care scene is the effort being made by the Bureau to maintain open channels of communication with the innovative health manpower developments and demonstrations currently taking place in various settings around the world. Experience has demonstrated that when properly evaluated and interpreted, these developments have important applications in finding solutions to many domestic problems of health manpower recruitment, training and utilization.

Also of serious moment is the increasing dependence of this country for its health manpower supply on professional personnel, particularly physicians and nurses, who have obtained their basic training abroad. A relatively small segment of this problem is made up of U.S. nationals who, unable to gain admission to U.S. medical schools, enroll in foreign educational institutions. A second and larger component is represented by foreign medical graduates who, seeking graduate training in U.S. hospitals presumably to prepare themselves better for practice in their homeland, prefer to remain in the U.S. on an indefinite basis. The third and now the largest component is made up of immigrant physicians and nurses seeking lifetime career opportunities in this country because of economic, social and professional advantages available to them here. These migration phenomena have important implication both to the countries of origin and to the U.S. On one hand they exert a serious skill drain. On the other, in the U.S., many of these physicians and nurses because of deficits in their professional preparation fail to meet U.S. standards of medical and nursing practice. These and related problems are under intensive study both domestically and in cooperation with appropriate international agencies and organizations.

The following sections detail the specific international activities of the Bureau by organizational units:

1. Office of the Bureau Director

a. Participation in and support of 4th World Conference on Medical Education, Copenhagen, September, 1972.

b. The Associate Director for Policy Studies served as Consultant on Health Manpower Planning to the World Health Organization, Geneva, September - December, 1972.

c. Participation in Canada-United Kingdom-U.S. Tripartite Conference of Health Ministers, Bethesda, March, 1973.

d. Participation in WHO-FIC International Conference on The Medical Assistant-Intermediate Levels of Health Care Personnel, Bethesda, June, 1973.

e. Development of working papers on health manpower planning, health manpower migration and health manpower training and technical analyses of agenda documents for U.S. delegations attending 1973 World Health Assembly and Regional Meetings of WHO.

f. Consultations and Conferences with visitors from abroad (WHO, Japan, U.K., Australia, Brazil, Sweden, West Germany, Iran, India, Israel, etc.)

2. Division of Physician and Health Professions Education

a. The Associate Director, DPHPE, participated as a consultant on general medical school management at a meeting of the Deans of Medical Schools in Africa sponsored by the World Health Organization in late November and early December 1972.

b. In addition, DPHPE Resources Staff gave consulting assistance on health facilities construction to visitors from Sweden, Greece, Switzerland, Uruguay, Canada, Great Britain, and France.

3. Division of Dental Health

a. International Collaborative Study of Dental Manpower Systems.

The World Health Organization (WHO) and DDH launched an international collaborative study of dental manpower systems in FY 1973. The six-nation study will analyze the characteristics of the methods employed for dental care delivery in the participating nations, stressing the manpower components of the systems and the effectiveness and efficiency of the systems when viewed from the perspective of the consumers and providers. Through the collection and analysis of clinical, administrative and sociological data, this three-year study will provide fresh insights into strengths and weaknesses of current national systems for providing dental services--insights which can benefit the United States as it seeks solutions to the dental health care problems facing it today.

In September 1972, at the WHO headquarters in Geneva, Switzerland, DDH staff, WHO staff and study coordinators from the six countries--Australia, New Zealand, Japan, the Federal Republic of Germany, Norway and Bulgaria--met for five days to discuss implementation of the study in their respective countries. Decisions were made concerning standardization of data collection procedures, team composition, schedules and collaborative interaction. In October, following the meeting of the study coordinators, designated research sociologists from the six countries met for five days with WHO and DDH staffs at the Fogarty International Center. This meeting resulted in further standardization of the sociological instruments, development of data collection procedures, and specification of translation requirements. Data collection began in Australia in January 1973, and in Norway in March. Data collection is scheduled for the four remaining countries in FY 1974.

b. Latin American Consultation on Dental Education

At the request of the Pan American Health Organization, Dr. Robert J. Lucas of DDH's Training Program provided advisory services for a three-week period in June 1973 to the Center for Research, Faculty of Dentistry, Federal University in Porto Alegre, Brazil, and to the University Cayetano Heredia in Lima, Peru. The services provided by Dr. Lucas focused on faculty and staff training in the application of audiovisual materials and training in methods of evaluation and measurement in dental education.

Also at the request of PAHO, similar consultation was provided by Dr. Lucas for a two-week period late in 1972 for the faculty of dentistry at the University of Panama in Panama City.

c. PL-480 Projects

Three projects carried out through P.L. 480 agreements in Israel were completed during the fiscal year, and final reports are being prepared. The projects were initiated when DDH had responsibility for dental materials and technology and dental epidemiology activities, and though it no longer has such responsibility, the agreements were honored and the work has been carried to completion. The completed projects are:

1) Clinical Evaluation of Dental Amalgam Restorations in Conservative versus Extended Cavity Preparations (Hebrew University, Jerusalem)

2) Clinical Comparison of Anterior and Posterior Restorative Materials in Paired Teeth, and Comparison of Constrasting Placement Techniques (Tel Aviv University, Tel Aviv)

3) Prevalence and Genetics of Oral Abnormalities Among Jews in Israel (Hebrew University, Jerusalem)

A fourth project related to the epidemiology of oral cancer in India is now in the data analysis stage and will terminate in September 1974.

4. Division of Nursing

a. The Division of Nursing represents to nursing in all parts of the world a central source of information and of expertise concerning all aspects of professional nursing. For this reason, nurses from Ministries of health, from schools of nursing, and from nursing organizations continue to seek guidance in planning their travel itineraries and spend varying amounts of time in consultation with appropriate members of our staff. During FY 1973, two large delegations, one from Japan and the other from Germany, visited the Division of Nursing for a general orientation of its program. Eleven other nurses spent from one to three days in the Division acquainting themselves in greater detail with aspects of this program which were of particular significance in carrying forward their responsibilities in their native lands. Conversely, nurses from this country seek guidance from the Division in planning professional visits to other countries.

b. Although the Division of Nursing is not presently involved in carrying out projects under P.L. 480, members of the staff represented the United States at international conferences of significance for program planning in this country.

c. The Director, DN, represented the United States at a Seminar for Nurses sponsored by the King's Fund College of Hospital Management held in London. The purpose of the Seminar was to compare developments in North America and in Britain on the deployment of nursing resources in the organization and provision of nursing care. Twenty nurses, ten from the U.K., seven from the U.S. and three from Canada, representing institutional and public health nursing, national nursing organizations, and governmental health agencies had intensive discussions around working papers submitted by the participants, as well as observations at one or more places where they could study their particular interests. Through correspondence and conversations among the participants since the conference, interest in the topics of discussion has been maintained and plans are under way for a second meeting.

d. In July 1973, the Director of the Division attended the first International Seminar in Nursing sponsored by the National League for Nursing in Israel. As a result of this seminar, there has been a continuing dialogue with Israeli nurses in strategic positions in education and service and a profitable exchange of information on issues of significance in both countries.

5. Division of Allied Health Manpower

The Associate Director for Program Planning and Evaluation, and the Chief of DAHM's Allied Health Professions Branch, participated in the First International Conference in the Health Sciences, which was held in The Hague, The Netherlands, October 8-12, 1972. The Conference was sponsored by The International Society for Education in the Health Sciences in cooperation with the Congress Bureau Inter Scientisa N.V., The Hague, The Netherlands. The Associate Director presented a paper entitled "Objectives in the Management of Health Manpower Education."

6. Division of Manpower Intelligence

a. Monograph on Foreign Medical Graduates (FMG's)

Publication and preliminary distribution of a monograph, Foreign Medical Graduates in American Medicine, was carried on in FY 1973

as part of a more extensive effort to compile, classify and analyze information on foreign health manpower in the U.S. health system. This overall effort is one important segment of the work in the Division of Manpower Intelligence (DMI) to determine the characteristics of the current manpower supply pool. Preliminary distribution of the approximately 300 copies of the original printing has been made. Delivery of the final printing of 3000 copies is expected by September, 1973.

b. Harvard FMG Study

This contract study has two parts. First, it attempts to improve the data base on foreign medical graduates by providing an estimate of the number of FMG's in a ten-year cohort not included in the records of the American Medical Association (AMA). The second part of the contract study is designed to assess the present activities of FMG's in the U.S. who are non-ECFMG (Educational Committee on Foreign Medical Graduates) certified. Both components of this study are efforts to clarify and expand present knowledge about a large component of physician supply in the U.S. (The eventual audience for results of this study will be the Bureau of Health Resources Development (BHRD) Program Divisions, other Federal departments (especially Immigration and Naturalization Service (INS), Department of Justice) professional organizations, education institutions and others.

c. PAHO Foreign Medical Student Survey

This pilot study was undertaken as a joint study with the Pan American Health Organization (PAHO) to determine the number of foreign students enrolled in medical schools in member countries of the Pan American Region of the World Health Organization (WHO) in academic year 1971-72. In particular, the age, sex, and year of study of U.S. citizens was surveyed. A preliminary report was submitted in mid-year FY 1973; the draft final report has been reviewed and the revised final report is expected shortly. (Results of the study may be disseminated to BHRD Program Divisions, Congress, professional organizations, education and training institutions and all other interested parties.) This study was undertaken to further the assessment of dynamics in the physician supply pool, particularly with regard to estimates of additions to future supply.

d. UNESCO Student Survey

As part of a worldwide medical student survey, UNESCO will undertake to determine the number of U.S. citizens enrolled

in foreign medical schools listed in the new WHO Directory of Medical Schools. Figures by age, sex, and class year will be collected for academic years 1972-73 and 73-74. This will complete the determination of U.S. citizens enrolled in medical studies outside the U.S. as part of the assessment of dynamics in the physician supply pool. The final contract was just negotiated for this study. (The eventual audience for the study report and data will be essentially that of the PAHO survey: BHRD Program Divisions, Congress, professional organizations, education and training institutes, and all other interested parties.

e. Planning and Evaluation Laboratory

Development of a planning and evaluation laboratory for the Regional University Center for Health Sciences in the Negev, Israel, is the focus of another contract study, included as one of a series of studies on aspects of health manpower or health manpower education in selected individual foreign countries. This series of studies is being carried out as part of a major effort to survey and analyze aspects of health manpower training and/or utilization in other countries which are relevant to U.S. efforts in these fields. The development of selection-admission criteria and innovative curricula and teaching methodologies and educational evaluation instruments are planned for the first year as well as the initiation of longitudinal study for the medical students to provide data for institutional evaluation at a later phase. Negotiation of this contract was just completed. The main target audience for the data reports, and other material generated by this study will be BHRD Program Divisions, professional organizations, and education and training institutes. Documents are being prepared for submission to the U.S. Israel Binational Foundation for possible funding for the continuation of this project in FY 1974.

f. Poland - PL-480 Project

Another component of the series of studies or aspects of health manpower in selected individual foreign countries is a study on health manpower planning in Poland to be financed through use of PL-480 funds. This will in turn form a part of the continuing analyses of developments in health and health manpower systems in other countries which are relevant to the U.S. This contract is still in the process of being negotiated; a draft study design was discussed and evaluated

on a recent site visit and a revised protocol will be submitted for review. Preliminary discussions have been held with Polish researchers concerning the feasibility of a study of the role of women in physician manpower in Poland. The main target audience will be BHRD Program Divisions, professional organizations and education and training institutes.

g. International Planning Monograph

A contract has been awarded for the preparation of a 500-page monograph on the structures, processes, and methods for health manpower planning in five industrialized countries of Europe with national planning systems reflecting a range of centralization (the U.S.S.R., the United Kingdom, Sweden, Finland and West Germany). This monograph is part of a series of international comparative studies of health manpower and health manpower education in other countries. This set of studies seeks to analyze and clarify experiences in other countries which are directly relevant to developments in the U.S. Special emphasis will be placed on planning for specialty and geographic distribution of health manpower, particularly physicians. This monograph will have as wide a target audience as possible, with special consideration for the Assistant Secretary for Health, Congress, State and local governments, professional organizations, and education and training institutes.

h. Comparative Studies

A contract to study patterns and the interrelationships of health manpower utilization, education, and licensing/credentials has also been awarded as part of the series of international comparative studies in health manpower. It will be carried out in Australia, Canada, Belgium, and Norway, and emphasis will be placed on comparisons and contrasts among the four countries and with the U.S. This study has several anticipated outputs: an annotated bibliography, individual country monographs, and a summary monograph with emphasis on the relevance for the U.S. of successful (or unsuccessful) patterns and developments in these countries. The target audience again will be as broad as possible, including especially BHRD Program Divisions, Congress, State and local governments, professional organizations, and education and training institutes.

i. FMG Bibliography

A 370-item bibliography, current as of September, 1972, was collected and indexed by keyword (KWIC) and source. Twenty-five hundred copies were printed as of November, 1972, of which

1500 were sent out on National Institutes of Health (NIH) mailing keys and another 200 through internal distribution and public requests. The primary audience was educational and training institutions, State and local governments, and professional organizations. This project was the initial internal effort in compiling and classifying information on foreign-trained health manpower in the U.S., as part of the broader DMI effort to determine the characteristics of the current problem of health manpower, especially physicians.

j. Quick Reference File

As another part of the effort to compile and analyze information on foreign-trained health manpower in the U.S., a comprehensive file on foreign medical graduates for easy entry and reference was developed and is being updated. It includes approximately 50 entries with basic statistical data on immigration, country of medical education, distribution and activities in the U.S., and other information useful in quickly replying to general questions. No published output is generated from this file; rather it is available for the use of DMI personnel to respond to queries from any governmental or non-governmental source. It is a helpful tool in the analyses of present characteristics of the physician supply pool.

k. FMG/SOAR (Supply Output and Requirements) Report

As part of the overall SOAR report and contribution to a Comprehensive Health Manpower Study, a draft report of some 170 pages (including almost 50 tables) and three appendices was prepared and circulated to over 20 reviewers for detailed comment and critique. This FMG report presented detailed background material and statistics on the place and utilization of foreign-trained physicians (both U.S. and foreign born) in the U.S. health care system together with a description of certain policy options and action alternatives which government and/or private and professional organizations may consider. An analysis of some of the issues which would have to be confronted in adopting the various alternatives is included. Written and verbal critiques from all reviewers were collected and synthesized, and in response to these comments an interim report of about the same length (but expanded in some areas and condensed in others) is being prepared. The initial direct audience for the report will be the BHRD/OD, Office of the Assistant Secretary for Health, the governmental and non-governmental reviewers and the agencies and professional or educational institutions they represent. In the end, the interim and/or final report will be targeted to a much wider audience including Congress, State and local governments and

perhaps the public. This particular FMG effort has been done as part of the overall DMI project to undertake special analyses of critical issues, in turn as part of the analytic studies done for Federal health manpower policy formulation and planning.

1. International Migration Bibliography

As part of the effort to compile, classify and analyze information on international health manpower per se, a bibliography on the international movement of health manpower, particularly physicians, has just been initiated. This would be expected to buttress the work of surveying and analyzing developments in health manpower in other countries relevant to the U.S. and would be something of a companion document to the already existing bibliography on foreign medical graduates in the U.S. It would be one part of the Bureau's information exchange effort. Collection of material has just started and consists primarily of gathering older bibliographies on the same topic, contacting WHO for citations known to them, and preliminary reviews of the latest indices to the literature. The target audience in this instance would be the Office of the Assistant Secretary for Health, other Federal departments, Congress, professional organizations, education and training institutes, and other public and international agencies.

m. Directory of Researchers

Another element in the compilation and analysis of developments in international health manpower is the establishment and maintenance of a roster of researchers and a directory of ongoing research in international health manpower. This would be related to the general DMI efforts to analyze the manpower aspects of health systems in other countries, as part of the Bureau information exchange system. Only the first step has been taken, with a rudimentary list of potential consultants and collaborators in selected countries where the Bureau has or may have international studies of various sorts. The beginnings of a list of U.S. personnel with health or health manpower expertise in specific countries is also developing. Present users of such a list, in its very limited form, would be only BHRD/OD, BHRD Program Divisions; eventually it might be more widely available.

F. THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES.

1. Environmental Health Program with the U.S.S.R.

The following activities were carried out in accordance with the March 1972 agreement on a general protocol for cooperative work in the area of environmental health sciences.

a. In August 1972, during the visit of the U.S.S.R. Ministry of Health delegation to the U.S., plans for implementation of the program were further discussed.

b. In September 1972, a delegation headed by Dr. Rall and comprising in-house scientists and a consultant, attended sessions of the XVI All Union Congress of Hygienists and Public Health physicians in Moscow and visited Soviet Institutes working in areas of mutual interest. Inhalation toxicology, biomedical effects of microwave exposure, and other environmental health effects were given particular attention.

c. In January 1973, a U.S.S.R. delegation, headed by Dr. Sidorenko, paid a two week visit to the U.S. Working sessions at NIEHS formulated a detailed plan of collaborative investigations. The delegation also visited other U.S. laboratories engaged in environmental health sciences. The following topics were incorporated into the program:

1) Study of quantative relationships of dose-time effect for biological prediction;

2) Prediction of the biological effect of chemical substances on the basis of their chemical structure;

3) Study of the mechanisms and indices of harmful effects of certain chemical substances on the CNS;

4) Study of the general principles of toxicological dynamics of chemicals;

5) Study of the combined biological effect of chemical substances introduced simultaneously;

6) Development of more rapid methods of assessment of biological effects of chemical substances;

7) Study of the allergic effects of chemical substances;

8) Study of the relationship of toxicity to physiochemical properties of compounds;

9) Study of long-term effects of environmental chemical agents;

10) Development and improvement of assessment method for combined and complex effects of pollutants;

11) Study of the complex effect of pesticides in relation to movement through the environment.

d. In June 1973, a team of three scientists, headed by Dr. Albert, Institute of Environmental Medicine, New York University Medical Center,

visited the laboratories of Dr. Bokina, A. N. Sysin Institute of General and Communal Hygiene, U.S.S.R. Academy of Medical Sciences, in relation to several of the topics listed above.

2. U.S. - U.S.S.R. Agreement on Cooperation in the Field of Environmental Protection

The Agreement, signed in Moscow on May 23, 1972, and the Memorandum of Implementation signed on September 21, 1972, provide for cooperation in eleven environmental projects, each with subprojects. Of these, Project VII, Part 2 -- Biological and Genetic Effects of Pollutants -- is of particular importance to NIEHS. Dr. Rall (NIEHS) and Dr. Shy (EPA) are co-chairman for this subproject.

A team of three Soviet scientists, headed by Academician Dubinin, visited the U.S. in June 1973, to review on-going work in three of the five categories listed under this subproject. EPA was given the lead in the category of epidemiology, and NIEHS in those of mutagenesis and heavy metals. In addition to NERC-RTP and NIEHS, the team visited other centers sponsored or supported by the two agencies. Agreement was reached on exchange visits for the development of collaborative studies.

3. Panel on Methods for Evaluating Environmental Mutagenesis and and Carcinogenesis: U.S. - Japan Cooperative Medical Science Program

The Panel on Methods for Evaluating Environmental Mutagenesis and Carcinogenesis was created in August 1972. The following activities were undertaken in relation to this Panel:

a. Dr. Frederick J. de Serres, Chief, Mutagenesis Branch, NIEHS-NIH, participated in the inaugural meeting of the Japanese Environmental Mutagen Society, which was held in Kyoiko Kaikan Hall in Tokyo on August 21, 1972. Following this meeting, Dr. de Serres attended the Eighth Meeting of the Joint Committee, U.S.-Japan Cooperative Medical Science Program, which was convened in Tokyo on August 24-25, 1972. At this meeting establishment of a Seventh Panel on Methods to Evaluate Environmental Mutagenesis and Carcinogenesis was approved; Dr. de Serres and Dr. Tadashi Yamamoto (Institute of Medical Science, University of Tokyo) were named Panel Chairmen. Following this meeting, Dr. de Serres participated in a conference on "Methodology to Detect the Genetic and Carcinogenic Potential of Environmental Chemicals," which was held in the Ministry of Foreign Affairs Building in Tokyo from August 25-27, 1972;

b. In May Dr. de Serres visited with Dr. E. M. Cohen, Director of the Medical Biological Laboratory TNO in Rijswijk, The Netherlands, and with Professor F. H. Sobels, Chairman of the Department of Radiation Genetics and Chemical Mutagenesis, State University of Leiden, The Netherlands. Following these visits, Dr. de Serres attended the council

meeting of the European Branch of the Environmental Mutagen Society (EEMS) as a representative of the American Branch of the Environmental Mutagen Society in the Biomedical Center of the University of Uppsala, Sweden, on June 3, 1973. Following this meeting, he attended the Third Annual Meeting of EEMS on June 4-7, 1973, and presented an invited lecture on "Hycanthone Chemotherapy - An Unresolved Toxicological Dilemma".

4. Investigation of Inhaled Pollutants Under the U.S.-French Agreement for Scientific Cooperation

In May 1970, an agreement was reached between NIH and the Institute National de la Santé et de la Recherche Medicale (INSERM) for the inauguration of ten programs of cooperative research, principally through the exchange of scientists for short periods by mutual inviation. No. 8 in the list was entitled "Basic reactions of pulmonary tissues to inhaled pollutants." NIEHS was given the responsibility for implementing this program with Dr. Sadoul, Nancy as the French coordinator. The following activities were carried out under this program in the fiscal year:

a. Dr. John H. Knelson, Environmental Protection Agency (EPA), was selected by Dr. Sadoul as the U.S. invitee to France. He spent the period February 12 to March 19, 1973, in France, Germany, and Scandinavia combining activities under this program with some representation of EPA at scientific conferences. He interviewed several of the leading authorities on environmental pollution in France, and laid the groundwork for future collaboration.

b. Dr. Q. T. Pham, Unité de Recherche de Physio-Pathologie Respiratoire, Nancy, spent the period April 30 to June 14, 1973, visiting a number of laboratories and organizations in the area, Boston - Ann Arbor - Research Triangle Park (RTP), actively engaged in the study of respiratory responses to environmental agents. He established a wide range of very important contacts from which he can develop collaborative efforts in the future.

5. Cooperation with the World Health Organization

a. As requested in December 1972, NIEHS prepared draft criteria on mycotoxina, Publications on Cadmium Poisoning (PCBs), and asbestos, to serve as background material for international criteria being prepared by WHO.

b. In March 1973, the Director General asked that DHEW detail Dr. Hans L. Falk to WHO for eleven months beginning in June 1973, to work on the development of international environmental health criteria, and following that to serve for four months with the International Agency for Research on Cancer, in Lyon. Dr. Falk left for Geneva in June 1973.

6. International Visits

a. At the request of the International Agency for Research on Cancer, Lyon, Dr. Rall participated in the Working Group on the Evaluation of the Significance of Mouse Liver Tumour Induction in Carcinogenicity Testing, October 5-7, 1972.

b. Dr. Insu P. Lee attended a meeting of the European S ciety for the Study of Drug Toxicity in Zurich, June 18-20, 1973.

c. The Environmental Protection Agency requested NIEHS participation in the Central Theme of Ecology and Environmental Deterioration, AAAS-CONACYT Conference on Science and Man in the Americas, June 29-27, 1973. Dr. Douglas H. K. Lee collaborated with Dr. Vaun Newill, EPA, on a pair of presentations dealing with general and specific problems of environmental pollution respectively.

G. THE NIH ROLE IN PARTICIPATING AGENCY SERVICE AGREEMENTS

Bangladesh - Cholera Research Laboratory (CRL)

The Cholera Research Laboratory (CRL) in Dacca, Bangladesh, continued operations during FY 1973, with funding mainly from the U.S. Agency for International Development (AID) and management by the U.S. National Institutes of Health/National Institute of Allergy and Infectious Diseases (NIH/NIAID). The Laboratory, formerly known as the SEATO Cholera Research Laboratory,was created December 30, 1961 by an amendment to a formal agreement signed by AID and the Government of Pakistan in October 1960. This amendment provided for the development of an autonomous international laboratory to be established at the Institute of Public Health in Mohakhali, Dacca, East Pakistan. The Laboratory was developed and became well known for its contributions to the understanding of cholera and diarrheal diseases. The work was temporarily interrupted in 1971 with the outbreak of civil disturbances, but the local staff remained on duty and managed to provide patient care services.

With the advent of the Government of Bangladesh, the Laboratory was placed in a caretaker status and funding provided by AID through the International Rescue Committee (IRC) based in New York. In April 1972, negotiations began between the Governments of the United States and Bangladesh for a new agreement for the continuation of the research program at CRL. An "Outline of Understanding" has been negotiated at the technical level and will be the basis for current operations.

The CRL is financed principally by AID, with lesser amounts from other sources. This includes funds made available to NIH by AID through a program agreement; direct AID support and through IRC; direct support from the National Institutes of Health and the Center for Disease Control (CDC), and with Bangladesh taka contributions in cash and utility support. The United Kingdom and other countries have also contributed funds, equipment

and services. The Johns Hopkins University International Center for Medical Research, (ICMR grant) has supported one guest worker at the Laboratory.

The NIH responsibility for the CRL has been effected by recent administrative changes. During FY 1973, these responsibilities were placed on the Geographic Medicine Branch (GMB), NIAID, and the Cholera Advisory Committee, which formerly shared CRL responsibilities with NIAID, was abolished. The GMB now coordinates the cholera program interests of the U.S.-Japan Cooperative Medical Science Program (CMSP) and of the former CRL. NIAID has a high program interest and commitment of dollars to the cholera research and is providing a staff member at the CRL in Dacca and two employees with the U.S.-Japan CMSP.

The CRL has remained functional during the year. Dr. David Nalin from the Johns Hopkins ICMR has continued to work throughout the year. His studies on oral therapy indicated that sucrose is not a suitable substitute for glucose for general clinical use. Dr. Stephen Richardson from the Bowman-Gray School of Medicine in Winston-Salem, N.C., spent six months at CRL. He and Dr. Nalin made a comparison of the toxins of E. coli and Vibrio cholerae in dog jejunal loops. Their findings indicate there is an antigenic relationship between the protein toxins produced by these two bacteria. This work is being continued by Dr. Bhattacharjee in the Bacteriology Branch of CRL.

The cholera epidemic was very mild this year. Shigellosis, however, has become a major cause of diarrhea among the patients seen at CRL. Dr. Mijibar Rahaman has started a search for enterotoxin from the isolates. Dr. K.M.S. Aziz is investigating the toxigenic capacity of Mycrosystis aeruginosa, a common organism of stagnant water in Bangladesh.

Dr. George Curlin, of the Epidemiology Division at the Center for Disease Control spent 6 weeks at the CRL. He repeated the trial of monovalent Ogawa and Inaba vaccines in the Matlab area, but there was so little cholera during the year no information on efficacy was obtained. He also initiated a limited census of the vaccine trial area to determine if there have been any significant changes in the population since the last survey. Mr. K.M.A. Aziz has designed and initiated a study in the Matlab area to obtain a chart correlating age with tooth eruption in children. This study utilizes information from children with recorded birth dates in hopes of getting information which can be applied to those without recorded birth dates. The United Nations conducted a second nutritional survey in Bangladesh and included children in the Matlab vaccine trial area. The results were published by the United Nations Relief Operation in Dacca in Information Paper No. 21.

The pending completion of a new intercountry agreement will assure the continuation of the CRL and planned programs. Plans have been made for a pilot study of the new cholera toxoid. The toxoid is being produced under the guidance of the Cholera Panel of the U.S.-Japan CMSP.

Testing protocols are being reviewed and the toxoid is expected to be ready for field trial in the summer of 1974. Continued financial support by AID has been assured and plans are proceeding for appropriate staffing of CRL. Two epidemiologists will be assigned to CRL by CDC, one of whom will be Dr. George Curlin. Dr. Ruth Hare has retired and Dr. Kendrick Hare, Director of CRL, has announced his intention to retire. A search committee for a new director is functioning.

H. THE MIDDLE AMERICA RESEARCH UNIT (MARU)

The Middle America Research Unit (MARU) is a research facility located at Balboa Heights, Panama Canal Zone, engaging in field and laboratory studies of the epidemiology and ecology of important virus infections endemic to Central and South America. MARU is currently operated by a private organization under contract to NIAID. Under this administrative arrangement, these various studies are being pursued directly and through informal collaboration with more than 20 different scientists and other institutions. Training opportunities in specific virological techniques also were afforded to six Latin American scientists and technicians during FY 1973. Because many of these diseases and the serious problems they pose are not confined to the tropics, the research at MARU may also serve to safeguard the health of United States citizens.

Highlights of research findings included the following:

1. Tacaribe Viruses

A high passage strain of Machupo virus was purified and shown to infect but not kill guinea pigs and marmosets. Protection against subsequent challenge of these animals with virulent virus was found to be complete. The candidate vaccine virus was adapted to grow in human diploid cell cultures and found to be temperature sensitive at 41°C. These and other markers will be used to derive virus clones giving optimum antigenic yield while retaining biological attenuation. Inactivation and immunogenic studies are contemplated.

Reciprocal testing of two Tacaribe viruses and two geographic races of Calomys callosus, rodents from which these agents were originally isolated, showed that immune tolerance and chronic viremia infection depend upon highly specific factors (probably the mosaic of membrane antigens) unique to both host and parasite. In addition to the theoretical implications, these results permit more precise planning of future attempts to isolate the presumptive virus which causes Korean hemorrhagic fever.

2. Venezuelan Equine Encephalitis (VEE)

Our basic hypothesis concerning the relationship between antigenic variation of these viruses and virulence for equines of the various strains was further substantiated by experimental inoculation of horses with other isolates. In addition, a strong correlation between equine virulence and

two in vitro markers, virus plaque diameter and optinum pH Hemagglutination, was established by systematic study of the latter properties in nearly 160 distinct strains. These data provide a strong base of reference for attempts to devise more sensitive techniques for antigenic separation of VEE viruses.

The pathogenesis of avirulent and virulent VEE viruses in horses was determined by serial sacrifice of animals infected by administration of virus by different routes. Multiplication of both types of virus in lymph nodes, thymus, spleen and marrow occurred. Virulent strains grew much better than avirulent ones, a phenomenon at least partly reflected in observed viremia levels. But both types of virus caused encephalitis and death when given intrathecally. Avirulent virus did not escape the brain under these conditions whereas virulent virus did. Comparison of cerebrospinal fluid levels of virus attained by each type of virus after both routes of inoculation, the regular appearance of antibodies and disappearance of circulating virus when animals become encephalitic and the finding of complement depression in some animals were suggestive that natural differences in virulence of VEE strains depends on a) a differential potential for replication in peripheral lymphoid tissues which somehow leads to b) high viremia and the rapid onset of an immune-mediated specific vasculitis with clinical expression in the brain.

3. Viruses of Phlebotomine sandflies

Six new members of the Phlebotomus Fever arbovirus group were characterized. At least one of these was shown to produce infection in man. The host-virus specificity of previously documented transovarial transmission of VSV-Indiana virus by L. trapidoi was demonstrated by failure of this sandfly species to support replication of two other VSV virus types. Significant progress was made toward large scale colonization of L. trapidoi. We should soon be able to use this species for experimental testing of its vector potential for a wide range of microorganisms.

4. Other arboviruses

Geographic patterns of past dengue virus infection of man in Central America were determined. As expected, the great majority of persons presently living in this 6-country region are now completely susceptible to infection. Further evidence for past activity of dengue type 1 virus was obtained.

Entry of sylvan yellow fever into eastern Panama from Colombia was restricted to May-December of 1970. Strong circumstantial evidence that this has reached the Bayano River basin less than 75 miles from Panama City was obtained in March of 1973. Since Aedes Aegypti is thought to have reinfested the city within the past year, major efforts to detect the presence of YF virus in the Bayano area are in progress in cooperation with workers at Gorgas Memorial Laboratory.

5. Hepatitis

A subgroup of patients having no evidence for either Hb A or Hb B virus infection has been defined. Materials from these persons are carefully stored for use in further attempts to define etiology. Exposure to Hb B virus was found to differ among three Indian tribes in Panama. Forest dwellers had high antibody frequencies, although one tribe had a higher incidence of chronic infection than the other. An island dwelling tribe had low incidence of antibody. Preliminary results suggest that infection by other enteric viruses parallels the Hb B patterns in these Indians.

Antibodies to Hb B were found in up to 40% of sera from several distinct Panamanian monkeys. The RIP test was used. If confirmed by passive hemagglutination, these data have important epidemiological significance for the natural history of this human disease.

6. Other studies

Angiostrongylus Costaricensis, a parasite of wild rodents which can cause appendicitis and acute enteritis in man was found for the first time in Panama. Cotton rats were most commonly infected but the worm was recovered from four other species as well. Studies of the behavior of this parasite in monkeys have been initiated and efforts are underway to locate human cases in Panama.

As part of our continuing cooperation in a WHO world-wide influenza surveillance program, we recovered virus strains during a local epidemic that occurred in September-October 1972. These proved to be related to the A_2/England/72 variant and were the first such isolates obtained in the Americas. Prior infection with the A_2/Hong Kong/68 virus conferred strong protection against illness caused by this new variant.

I. THE U.S. - JAPAN COOPERATIVE MEDICAL SCIENCE PROGRAM

The U.S. - Japan Cooperative Medical Science Program was the product of a January 1965 meeting of the heads of state of the United States and Japan. The mutual concern for the health and well-being of people in underdeveloped countries prompted the two leaders to agree to undertake jointly a cooperative medical research effort focused upon health problems of recognized importance in Asia. The relevant regions in Asia are not specifically defined, but are generally understood to include the Republic of Korea on the north, India and Pakistan to the west, and other adjacent nations in the broad Pacific basin.

The implementation of this program involved the time and effort of prominent medical scientists of both countries to identify and define specific parameters of the disease categories to be included in the new Program. From this group of scientists evolved the Joint U.S.-Japan Cooperative Medical Science Program Committee which meets annually,

alternating between Japan and the United States, to review the Program's objectives, operations and accomplishments, and to initiate new management policies and procedures. The most recent committee meeting, the ninth, was held at the National Institutes of Health on July 26 and 27, 1973. During this meeting, the program reviews of two panels, tuberculosis and cholera, were completed, and the reviews of two additional panels, malnutrition and viral diseases, were initiated. This program is administered for the United States by the Geographic Medicine Branch, the NIAID, NIH.

1. Cholera

Development and evaluation of a cholera toxoid for human use continued to receive major contract support. A method was developed for large scale production of highly purified cholera toxoid containing only trace amounts of somatic antigen. Substitution of glutaraldehyde for formalin as the toxoiding agent has resulted in a more stable, but less immunogenic toxoid, which can be satisfactorily absorbed on a protamine-aluminum phosphate adjuvant. A current study in volunteers has shown that this toxoid causes almost no untoward reactions in contrast to formalinized toxoid. Circulating antitoxin levels, however, have been lower than those obtained with comparable doses of formalin toxoid and it is not yet clear whether the loss of immunogenicity can be satisfactorily overcome by increasing the toxoid dose and by enhancing the response with adjuvant. Dogs immunized with this toxoid both parenterally and by parenteral priming dose followed by an oral booster were protected against oral challenge with living vibrios. In man, however, we do not know what level, if any, of either systemic or local antitoxin will provide protection against natural exposure to cholera, and the answer to this question will come only from a properly controlled field trial. A pilot study, designed to determine responses to this toxoid in a cholera endemic area, will be started soon in Bangladesh, in preparation for a major field trial in the coming year.

The panel has supported basic studies in a number of areas. It is now clear that the probable binding site for cholera enterotoxin in the epithelial cells of the bowel is a specific neuraminidase-resistant, monosialosyl ganglioside. This suggests that cholera neuraminidase may increase susceptibility to cholera by converting sialidase-sensitive gangliosides to the more avid toxin receptor during the course of disease. Studies on mechanisms of antibacterial resistance suggest that complement-independent antisomatic antibody capable of inhibiting both the mobility of vibrios and their absorption on the mucosal surface may play important roles in immunity to cholera. At a practical level these findings suggest that the ultimate optimal immunogen will contain both somatic and toxoid antigens.

A number of laboratories are investigating the enterotoxins of Escherichia coli and have demonstrated similarities between the heat-labile enterotoxin produced by this organism and the cholera enterotoxin. The role of the heat-stable enterotoxin in pathogenesis is not at all clear. Genetic

studies have now demonstrated clearly that the capacities to produce both heat-stable and heat-labile enterotoxins by E. coli are transmissible by conjugation by separate specific non-chromosomal DNA's residing in episomes. A similar mechanism in cholera has not yet been revealed.

Toxic substances from non-cholera vibrio's have been isolated and purified and are being studied for their biological properties and activities.

2. Leprosy

This past year, the U.S. Leprosy Panel has seen advances in pharmacology, immunology, and cultivation. In pharmacology, the early effects of the three-year mass chemoprophylactic treatment for leprosy with acedapsone (DADDS) in the isolated Pingelapese population are now being seen. DADDS is a repository type derivative of the standard antileprotic drug, dapsone, (DDS). The findings of the second annual surveillance of the population are as follows: three persons developed leprosy two years after the DADDS injections were discontinued in the general population. The expected number of annual cases in the untreated population is twelve. Persons coming down with leprosy had received less than ten injections. There have been no cases of leprosy observed in people who received all fifteen injections. Two or three injections of DADDS does not appear to prevent the onset of leprosy in persons about to develop the disease. Three of four injections of DADDS, however, suppresses the onset of the disease for the duration of the injections and for about 6-12 months thereafter. From this it would appear that there is a threshold number of injections of DADDS for leprosy prophylaxis.

New cases of leprosy are being treated with DADDS and surveillance of the entire population is planned through 1980. If the DADDS chemoprophylaxis proves to be effective over the long term, DADDS will significantly facilitate the therapy of leprosy patients in endemic areas with limited medical and public health capacity.

In continuing studies of the metabolism of DDS and the phenotypic classification of subjects according to acetylation characteristics, recent results suggest some association between M. leprae resistance and intermediate and fast acetylators. An increased rate of clearance of DDS and MADDS from the plasma was also related to DDS resistance.

The chromatographic-fluormetric procedures for the measurement of DDS, MADDS, and DADDS have been improved. It is now possible to detect as little as 0.1 to 0.2 ng/ml of plasma. This can be accomplished in one run, instead of the two previously required, with a 50% reduction in total analysis time.

Two chemotherapy trials (D663 II and rifampin I) have been completed, and a report is being prepared recording the final results. The data of the B663 II

trial of 48 patients demonstrated that the daily regimens were more effective than the intermittent ones. The skin pigmentation side effects and ENL (erythema nodosum leprosum) reactions will be described fully in the publication.

In the rifampin I trial, the efficacy of rifampin against M. leprae was compared with DDS in untreated lepromatous patients. The viability of M. leprae from biopsy specimens was studied by the mouse footpad test.

The results show that biopsy specimens from patients treated with daily refampin were negative in three months, whereas the specimens from the DDS treated group were not negative until six months. The therapeutic effect of intermittent rifampin and DADDS is now being studied. This type of rifampin regimen is more desirable, since rifampin is expensive and effective intermittent therapy is more practical in underdeveloped countries where leprosy is endemic. The combined therapy might also reduce the likelihood of patients developing drug resistance.

Progress in the area of immunology has continued. Encouraged by the results of single injections of transfer factor into lepromatous patients. the U.S. Leprosy Panel has designed a transfer factor protocol for further studies of the immunologic deficiencies noted in leprosy.

Encouraging results with the thymectomized-irradiated mouse as an animal model for leprosy research continued throughout the year; however, the problem of reduced longevity has not been solved in this immunological defective animal.

An efficient method for the production of antilymphocyte serum (ALS) has been developed, and a means for testing the potency has been standardized. This product is available to approved investigators through a service contract.

Some encouraging reports have come from the continued efforts to cultivate the leprosy bacilli. There is evidence that M. leprae grows readily in some armadillos, producing a disease condition similar to that in man. It is very possible that this animal could be a valuable source of biopsy material for leprosy research. Human skin biopsy specimens with large numbers of M. leprae are now provided by the U.S.-Japan Program.

3. Malnutrition

Additional data confirm earlier reports that severe malnutrition during the first two or three years of life, even though dietary adequacy is later provided, has a lasting detrimental effect upon intelligence and behavior in later life. It is anticipated that highly sophisticated neuropsychiatric and neurophysiologic methodology currently being developed and applied will provide the basis for more exacting quantification of brain functions and allow more precise evaluation of the influence of early malnutrition thereon.

There has been a dramatic fall in morbidity rates from infectious diseases observed in children receiving both nutritional supplements and medical care. This was not seen when medical care alone was provided. Better control of infections which so commonly thwart recovery from sever malnutrition in infancy are under careful study.

Also under investigation in several countries is the prevalence and frequency of iron and protein deficiency in children and of folic acid deficiency in pregnant women. Other research in progress endeavors to explain, and find means of correcting, the poor absorption of iron from cereal grains.

Work continues in an attempt to incorporate a high level of protein into commercially produced rice in Southeast Asia. The biological quality of rice protein is fairly high and an increase in the protein level in rice would go far toward alleviating protein undernutrition in countries for whom rice is the mainstay of subsistence. Based on recent breeding work involving progeny of successful crosses between six high-protein strains and IR_8, the consensus is that the protein content of the new rice is a genetically determined characteristic. Four of the six strains contain 10 1/2 per cent protein which can be pushed to 12 per cent under optimal conditions of growth. Breeding experiments are in progress to incorporate into the strains resistance to certain plant diseases. The human nitrogen balance studies using one of the high protein rice varieties in adults were so encouraging that the same type of study will be done in rapidly growing infants and preschool children in the Philippines.

4. Parasitic Diseases

Research under the Parasitic Diseases Panel is confined to two parasitic infections of very great importance in Asian Countries - schistosomiasis and filariasis.

a. Schistosomiasis

Studies have continued in gaining an understanding of the mechanism of immune response in schistosomiasis. It has been shown that two anti-schistosomal drugs, tartar emetic and niridazole, suppress the schistosome egg granuloma *via* anti-inflammatory action. The role of anti-DNA antibodies in glomerulonephritis associated with human and experimental schistosomiasis is being investigated.

With the development of aseptic techniques a design of suitable media, work toward the objective of establishing a cell line of the snail host of *S. mansoni* has progressed. In addition, sporocysts of *S. mansoni* have undergone development to cercarial embryos in these *in vitro* snail cultures.

Chemotherapeutic studies have included development and testing of synthetic antischistosomal agents. Structural and conformational similarities of two effective compounds have led to a proposal that antischistosomal activity has the following requirements: a 5-nitroheterocyclic ring linked in the 2-position to a nitrogen of low basicity *via* a vinyl group. Another study has shown that tubercidin administered after its adsorption on to host red blood cells was schistosomicidal against both *S. japonicum* and *S. mansoni* in monkeys.

b. *Filariasis*

Further work has shown that the gerbil is the most useful rodent host for studies with the lymphatic-dwelling filarial worms. Base-line studies are continuing with the aim of using this host for evaluation of new filaricidal compounds.

Biochemical studies of several filarial species indicate that a few metabolic pathways are sufficiently different from the analogous mammalian counterparts to be potentially exploitable by appropriate kinds of drugs.

Efforts have continued to develop a vaccine composed of infective filarial larvae which have been suitably attenuated *via* irradiation.

Histopathological studies of *Brugia pahangi* in dogs have shown that both humoral and cellular response mechanisms rise and fall in intensity in correlation with molting and initiation of microfilarial deposition.

Studies of chemotherapeutic agents are being carried out to determine which metabolic systems are affected by specific compounds. Further critical research on filarial physiology needs to be done.

A workshop in "Factors Affecting the Competence of Diptera as Vectors of Arboviruses and Filariae" included discussions of the genetics of mosquito susceptibility, specificity and development of filariae in arthropod hosts, and population dynamics of mosquitoes.

5. *Tuberculosis*

In the past year significant advances have been made in the field of tuberculosis research. Much of this has been due to the cooperative efforts of a number of investigators and the availability of standardized, highly characterized mycobacterial materials produced through services contracts of the U.S.-Japan Program. Mycobacterial cell extracts and culture filtrates have been produced and disrupted under specified conditions. These materials will be used to isolate specific antigenic fractions which will eventually be studied for *in vivo* and *in vitro* activity and used in immunological research. Mycobacterial products such as BCG, PPD, and cell wall fractions are recognized as promising

immunological adjuncts in the treatment and prevention of mycobacterial diseases as well as carcinogenic and immune deficient diseases.

A reference system of mycobacterial antigen and antibody serum is now available. The system has been standardized and characterized by immunoelectrophoretic procedures.

Progress has been made in evaluating existing animal models for the study of tuberculosis vaccines. A sub-human primate model has been studied using aersolized BCG vaccination followed by an aersolized challenge. Dose-response data are now being collated.

6. Viral diseases

Research under the Viral Diseases Panel is limited to studies on rabies and on arboviruses with emphasis on dengue and the pathogenesis of hemorrhagic fever.

a. Rabies

Studies on antigenic relationships have shown that there are at least six different virus types from Africa which are serologically related to rabies virus. The newly studied rabies - relatives add to the serotypes available to test the capacity of these strains to broaden the immunity to rabies virus.

Survival time of infected mice was significantly prolonged by several methods of immunosuppression indicating that an immune mechanism is involved in the pathogenesis of at least one of the rabies serogroup viruses.

Work has continued on the isolation and characterization of the protective antigens of rabies virus. In addition, the role of adjuvants as augmenters of immunological response is being studied with the goal of administration of a massive dose of purified antigen attached to mineral adjuvant.

Also being developed are improved methods for the inactivation of rabies virus without significant loss of immunogenicity. Included were studies of the kinetics of beta-propriolactone degradation, refinement of assays for residual live virus and actual inactivation of virus by both formalin and beta-propriolactone.

b. Dengue

Various procedures have been evaluated for potential use in the diagnosis of dengue and in understanding its epidemiology. Area-treated CF antigen and standard sucrose-acetone antigens and dengue virus were compared. The former was more type specific but less sensitive than the latter.

The first comparative electron microscopic study of the four dengue virus types, propagated in vitro, has been completed. All dengue viruses appear to be spherical as they mature and the particle size of the four types is the same. The sequential stages of viral development and release for the four types of dengue virus, in infected cells, are quite similar.

Continuing pathological studies have involved the search for dengue antigen and immune complex in biopsied tissue of kidneys and skin and in autopsy material obtained from patients with dengue hemorrhagic fever. The blood vessels of the skin were the only sites where dengue antigen could be found in significant amounts in conjunction with complement. Circulating leucocytes were also found to harbor dengue antigen. Evidence has thus been obtained to support the hypothesis that the pathology and pathogenesis of vascular changes are related to immunological reaction.

Attempts are being made to establish an in vitro model of dengue infection. In vitro formed virus-antibody complexes are being studied to determine the effect of dengue virus of Raji cells in the presence and absence of antibody and complement. The hypothesis is that complement activation may be triggered by a simultaneous production of large amounts of virus and anti-dengue antibody during secondary dengue infection.

7. Environmental mutagenesis and carcinogenesis

There is expanding evidence that human health will be increasingly influenced by chemical pollutants introduced by man into his environment. The purpose of the U.S. Environmental Panel is to develop better methods to detect potential mutagens and carcinogens and to evaluate existing methodology.

The Panel met twice during the past twelve months, once in connection with the conference held in Tokyo in August and then again in February. Because of budget limitations, the primary activity has been to plan workshops and conferences and to develop mechanisms to stimulate research relevant to program priorities.

J. THE INTERNATIONAL CENTERS FOR MEDICAL RESEARCH (ICMR) PROGRAM

A program for the International Centers for Medical Research was established in 1960 by the National Institutes of Health "to advance the status of the health sciences in the United States and thereby the health of the American people" by expanding collaborative research between U.S. universities and selected foreign institutions and investigators.

The four grants funded under this Program are awarded for five years with continued support contingent upon program review at the end of each year of operation. One of the most important features of this program is that of long-term support, as contrasted with the transiency which has characterized a number of other international projects. This is a necessary

ingredient for the full development of university careers in science which will effectively utilize the international medical experience of individual scientists. A major advantage of this program is that it provides opportunities for established and highly competent investigators to utilize valuable research opportunities abroad without losing their university affiliations and faculty appointments. The long-term support of the ICMR's does not represent a form of foreign aid. Rather the primary objective is a collaborative effort in biomedical research of specific relevance to the health of the American people and to the U.S. scientific community. The four current ICMR grants were renewed for an additional five years beginning in FY 1970, and at the same time support to the LSU Center in San Jose, Costa Rica was phased out.

1. Purpose and Scope

The ICMR program has as its principal objective the provision of high quality research and scientific opportunities for Americans in the broad fields of geographic medicine, and in response to the special opportunities existing within each ICMR framework. The length of the research period overseas is a discretionary concern of the ICMR program director, and is obviously determined by both the interests of the prospective investigator and the specific opportunities available within the given ICMR unit. Consistently, the emphasis is upon the quality rather than the quantity or duration of the research programs.

The aggregate ICMR units are serving increasingly as a national resource for utilization by senior as well as less experienced scientists to create a comparatively modest pool of investigators with a sustained career interest in international or geographic biomedical research. In this regard, the ICMR program directors are encouraged to establish a selective, interdisciplinary scientific program. Their activities encourage and accommodate a number of parent university departments other than the department which primarily sponsors the ICMR operation. Particular advantage is taken of special strengths within the overall parent university, including opportunities in health-related fields outside of the classical confines of tropical medicine. Within the overall ICMR framework, the ICMR Research Associate Program (IRAP) functions. This centrally coordinated activity is specially designed to recruit investigators on a national basis and specifically from universities that do not have an ICMR.

As far as is possible, the ICMR core grant is used for research support at the off-shore ICMR site rather than at the parent, domestic university. In this regard it is accepted that some preparation preliminary to an overseas assignment is frequently necessary or desirable, and as many items of equipment and supplies as feasible are purchased in the United States.

2. Program

The four institutions participating in the ICMR program at present, and their respective areas of research interests are as follows:

a. Johns Hopkins University (Baltimore, Maryland)

Program Director: Dr. Frederick B. Bang

Johns Hopkins University with the participation of the School of Hygiene and Public Health and the Department of Medicine is collaborating with the Calcutta School of Tropical Medicine, the All-India Institute of Hygiene and Public Health, and the Postgraduate Institute for Medical Education and Research in Calcutta, India. During the past year scientific activities have also been initiated in Kathmandu, Nepal, and Dacca, Bangladesh, in anticipation of an eventual move from Calcutta. Program emphasis is directed toward the epidemiology and mangement of human diseases of large populations and the ecology and behavior of animals which live in comparatively close association with man.

Studies are in progress on the year-round distribution of respiratory and enteroviruses in normal children in rural communities. Other research includes the development of antigens for skin tests in leprosy, and the ecology of the economically important bandicoot rat (B. bengalensis).

Intensive biochemical research in cholera is also in progress. This work includes antibiotic and oral therapy, cholera in children, comparison of classical and El Tor cholera, and a number of very significant experimental pathophysiological studies.

b. University of California (San Francisco, California)

Program Director: Dr. J. Ralph Audy

The University of California with the participation of the Hooper Foundation, the School of Public Health, and the Medical School, is collaborating with the Institute for Medical Research, Kuala Lumpur, Malaysia, and the University of Malaya. This International Center continues to place strong emphasis on infectious diseases transmitted from animals to man. Because of the long standing research interest and experience in studying the fundamental problems of human ecology at the University of California, a collaborative program has been developed embracing medical zoology, microbiology and parasitology. The scope of this collaborative endeavor has now been expanded to include related socio-cultural research and medical genetics.

Long-term research projects in Malaysia and California are based on three general laboratory programs: the Arbovirus Research Unit, the Parasitology Laboratory, and the Medical Anthropology and Rural Health Research project.

The arbovirus research is focused on the epidemiology and ecology of dengue virus and the relationship of this virus to mosquito-borne hemorrhagic fever. A jungle reservoir (monkey) has recently been demonstrated for dengue. The parasitological research is based on studies of trematode ecology and interactions of various parasites in the snail host and the ecology of Malayan pentastomes or tongue worms. The snail trematode antagonism studies are directed toward the biological control of schistosomiasis, and this ICMR represents a leading world resource for this important field research. Invesitgators from this ICMR have also studied the histopathology of host reaction to acarine parasites, the relationship of monkeys to human malarial infection, and jungle cycles of scrub typhus, Q fever, and tick typhus.

Abundance, distribution, life cycles and ectoparasites of rodents closely associated with man have also been studied. Work on the possible role of the Indian fruit bat as a reservoir of human viral infections has been completed. Other field studies include the investigation of bacteria and viruses pathogenic for man in monkey populations. Socio-cultural studies concerned with Malayan attitudes toward health and nutrition and the influence of native and western practitioners of medicine upon these attitudes have been undertaken by a number of variously trained, medically oriented social scientists.

c. University of Maryland (Baltimore, Maryland)

Program Director: Dr. David F. Clyde

The University of Maryland with the participation of its School of Medicine, and collaborating with the Institute of Hygiene, Lahore, has undertaken a varied research program in West Pakistan. Comprehensive studies of arthropod-diseases have been undertaken. During FY 1971, a field unit in Salvador (Bahia), Brazil, was established at the Federal University of Bahia to study insect vector pathology as a tool for biologic control of malaria. Additional studies are planned in the area of schistosomiasis and vector genetics. Due to diverse factors, it is possible that the University of Maryland will eventually relocate their ICMR from Pakistan to Brazil.

More recent research in Pakistan includes studies of mosquito-borne viruses in man. In addition, a detailed investigation of several different clinical entities, e.g. bleeding disorders in humans, has been recently completed. Research on immunity in tuberculosis and on the relationship between cirrhosis, hepatitis-associated antigen, and viral hepatitis has also been completed.

Mosquito genetic investigations of a comparatively unstudied vector of Japanese encephalitis virus have been of unusually high scientific merit and promise. Knowledge about the genetics of this mosquito, Culex

tritaeniorhnychus, now approaches the abundance and high quality of information previously known about two other mosquito vectors of human disease. This new information has been sought to establish a scientific basis for the ultimate biologic control of human Japanese encephalitis. A new "compound chromosome" technique has been developed and is under consideration for early field application on a limited scale.

d. Tulane University (New Orleans, Louisiana)

Program Director: Dr. Paul C. Beaver

Tulane University, with the participation of the Department of Tropical Medicine and Public Health, other departments of the Medical School, and the Department of Anthropology and Sociology, is collaborating with the Universidad del Valle, Cali, Colombia. The research work is in two general areas: causes, prevalence and distribution of human diseases with human relevance, and physical environments which determine ill or well-being.

Parasitic diseases research has continued to focus principally around the following diseases: trypanosomiasis, malaria, filariasis, and amebiasis. The local epidemiology of Venezuelan Equine Encephalitis has been studied and documented following the recent epidemic. The Virus Group also has a continuing interest in rabies. A comprehensive clinical evaluation of bacterial meningitis treatment regimens is in process. Finally, the multi-disciplinary study of frustrated suicides has recently been continued and refined. New projects are concerned with maternal and child health, family planning, and include health services research.

K. NIH ASSISTANCE TO THE WORLD HEALTH ORGANIZATION AND THE PAN-AMERICAN HEALTH ORGANIZATION

The long history of cooperation between NIH and the WHO continued during FY 1973. Five NIH laboratories serve as Regional or International (Research/Reference) Centers for WHO. Some 42 NIH scientists serve as advisors/consultants to the WHO. The Director of NIH is a member of the PAHO Advisory Committee on Medical Research. The Directors of the NCI and the NHLI serve on the WHO Expert Advisory Panels, and the Director, Center for Population Research, NICHD, is a member of the WHO Advisory Group to the Expanded Program of Research, Development and Research Training in Human Reproduction. The Director, NCI, is a member of the IARC Scientific Council.

The Director, Fogarty International Center, served as a member of the U.S. Delegation to the 26th World Health Assembly. The Director, NCI, was the U.S. Delegate to the 11th and 12th Annual Meetings of the Governing Council of the International Agency for Research on Cancer.

The Director, NIEHS, participated in the meeting on environmental health criteria and standards. A number of staff members took part in the 4th World Conference on Medical Education sponsored by the World Medical Association in cooperation with WHO.

The National Library of Medicine continued in its program of assistance to the PAHO Regional Library of Medicine at the Federal University, Sao Paulo, Brazil. Staff members of the NCI met with representatives of the Office of International Health, and the Department of State to define the roles of such international cancer agencies as WHO, IARC, and the International Union Against Cancer. NIH, in collaboration with WHO, sponsored an international conference on medical assistants. Four NIH employees are on detail to WHO.

Review of technical documents, working papers, and other program materials has been requested by the Office of International Health to provide assistance and guidance to U.S. delegations to meetings of such organizations as the World Health Assembly, the PAHO Directing Council, the Health Ministers of the Americas, and the IARC.

L. UNITED STATES FELLOWS AND TRAINEES ABROAD

The sponsoring of U.S. Fellows and Trainees for Research and Training Abroad began with the establishment of the several institutes at the NIH. The criteria originally developed to select training locations for Fellows and Trainees provided that they might attend any qualified institution in the United States but study abroad was authorized when satisfactory evidence was provided that the type or quality of training abroad was particularly suited for their purpose and could best be obtained there. This program, which is administered by the individual institutes, began with one fellowship award made in 1947. The peak year for U.S. Fellows and Trainees abroad was FY 1966 with 397 awards. Since FY 1966 foreign training has been reduced due to budgetary controls. During FY 1973, 143 awards were made.

M. GUEST WORKERS

Under the Guest Worker Program, the NIH may invite individuals, other than employees or fellows of the NIH, who are sponsored by qualified organizations to utilize the research facilities of the NIH for the purpose of carrying on a research project or participating in a research program. The basis for acceptance of a guest worker rests on complementary professional interest, appropriate facilities, and the prospect of mutual benefit to the host Institute or Research Division and the guest worker. During FY 1973, 134 individuals worked at the NIH under this program.

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